THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 51 MARCH, 1944 No. 3

THE DEMONSTRATION OF PULMONARY LOBES AND INTERLOBAR FISSURES BY ROENTGENOGRAMS OF AN ARTIFICIAL THORAX

By E. M. MEDLAR, M.D., G. S. PESQUERA, M.D., W. H. ORDWAY, M.D., AND E. C. LASHER, R. T.

From the Hegeman Research Laboratory and the Metropolitan Life Insurance Company Sanatorium

MOUNT MCGREGOR, NEW YORK

IT IS the usual procedure to interpret the pathologic conditions observed in roentgenograms of the chest as being in the upper, middle or lower thirds of the pulmonary field, or in the hilar, central or lateral thirds. Such interpretations disregard the larger anatomical units, the lobes of the lung. Anyone who is familiar with the pathology of pulmonary tuberculosis in man should be acutely conscious of the importance of the large anatomical units of the lung, for in this disease the preponderance of dangerous cavitating lesions occurs in the cephalad or superior portions of the lobes, and tuberculous foci in the inferior or caudal portions show a very strong tendency to retrogress completely or to become small, firm, encapsulated lesions. Because of this peculiarity of pulmonary tuberculosis it is important to determine whether the initial lesions and the "spreads" of the disease are in the upper or the lower portions of the lobes of the lung.

The prominent position now held by thoracic surgery also calls for the location of pulmonary pathology in relation to the pulmonary lobes. If lobectomy is to be performed a preoperative location of the pathologic condition enables the surgeon to appraise the physiological after-effect dependent upon the volume of tissue to be removed. The removal of the relatively small right middle lobe, for instance, should not cause any undue over-compensation of the remaining lung tissue, whereas the removal of a large lower lobe might cause a serious physiological complication at a date far removed from the operative procedure. If thoracoplasty is under consideration and the pathologic condition can be demonstrated to be in the cephalic portion of the lower lobe, then it would seem to be a needless sacrifice of lung tissue to perform a total thoracoplasty when only a limited area need be compressed.

Before an interpretation of the relative position of pathologic conditions seen in roentgenograms of the chest is possible, it is necessary to demonstrate the limits of the lobes of the lungs and of the interlobar fissures in a three dimensional field in the normal chest. This is impossible because under normal conditions the interlobar fissures are not of sufficient density to cast a shadow that would demarcate the lobes.

It is well known from dissection of cadavers and from necropsy observations that interlobar fissures vary to a certain degree in both their extent and their position. For instance, the fissure between the upper and middle lobes of the right lung may vary from a small superficial depression to a complete separation of the lobes down to the bronchial tree at the hilum. Textbooks of anatomy offer little aid since the pulmonary lobes and their relation to bony landmarks are dealt with in a very sketchy manner. The absence of any satisfactory method of orientation at present makes it impossible to determine whether lesions in certain areas are present within a certain lobe or an interlobar fissure.

The only approach to a solution of this problem is upon an experimental basis. This was first attempted by Sampson, Heise and Brown[1] when they used wire gauze to locate the interlobar fissures inside the thorax of a skeleton and then took roentgenograms from various angles. Later Berry and Childs[2] attempted to demonstrate interlobar fissures in cadavers by

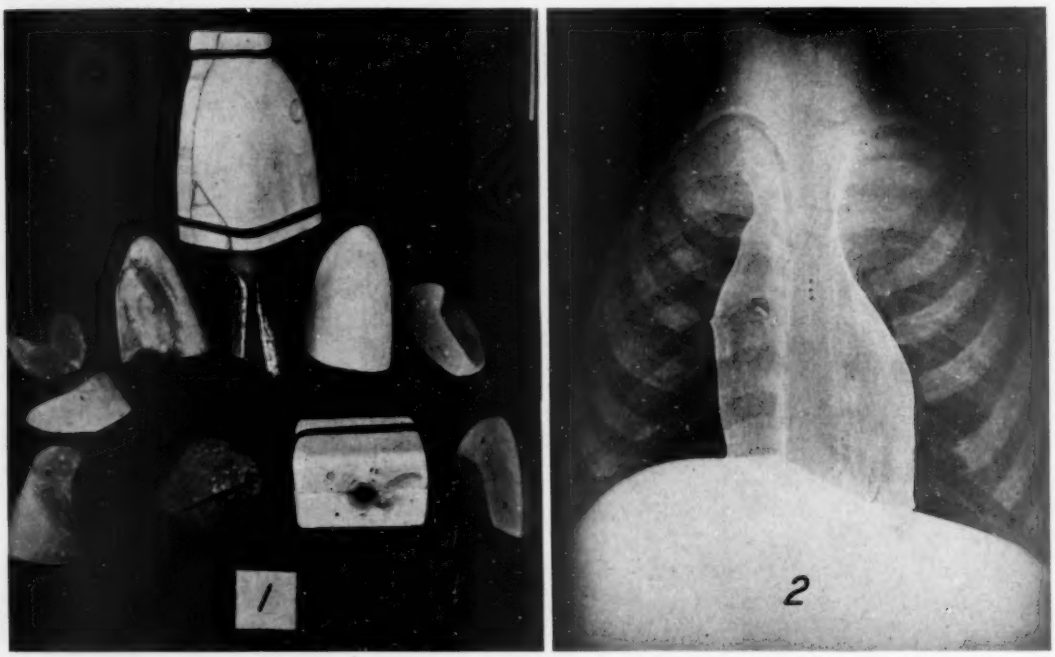


FIG. 1. This is an assemblage to illustrate the method of procedure and the casts used. At the top is the dummy set at an angle to show the anterior, posterior and lower divisions. It is assembled with the lung lobes and mediastinal contents in place and is ready for the taking of roentgenograms in any position desired. Just below the dummy is a paraffin cast of the mediastinal contents with the pleural surfaces covered with lead foil. To the left is the master plaster cast of the right lung as it appears from a medial view and to the right is the left lung as it appears from a lateral view. Below these structures there is a latex mold of a lobe of a lung and a mold assembled for the pouring of a cast of a lobe. Paraffin casts of the lung lobes are shown at the side—the three lobes of the right lung to the left and the upper and lower lobes of the left lung to the right. Throughout the study paraffin casts of the mediastinal contents and of lung lobes were used.

FIG. 2. A posteroanterior roentgenogram showing the mediastinal contents covered with lead foil. When considered *en masse* the trachea and main bronchi, the esophagus, the heart, the large arteries and veins, and the areolar and adipose tissue form a considerably greater bulk than is generally realized when viewing the usual chest roentgenogram. The apparently large size of the mediastinal contents as shown in this roentgenogram emphasizes that fact. If the appearance portrayed here is kept in mind when the other roentgenograms are studied a clearer conception of the various structures shown will be obtained and the blocking out by the mediastinal contents of certain portions of fissure and lobes can be appreciated.

Fig. 3. A posteroanterior roentgenogram with lead foil placed in the three interlobar fissures. Note that in this pair of lungs the interlobar fissure on the left side is highest at the level of the fourth rib at the posterolateral part of the chest, while the analogous fissure on the right reaches its highest point at the level of the fifth rib at the costovertebral junction. The fissure between the upper and the middle lobe of the right lung has a slight upward concavity and extends almost horizontally at the level of the third rib ventrally. At full inspiration this level might readily be at a level between the third and the fourth ribs. The fissures follow the contour of the mediastinal contents and the major fissures extend down to the diaphragm. The two horizontal lines are drawn at the level of the fourth and the sixth costovertebral junctions and represent horizontal planes through the chest. The first rib shows only as a light line in this roentgenogram because of the angle at which the outline is pointed on the pleural surface. These points were chosen because they remain stationary, while the position of the ribs and the sternum changes somewhat during the process of breathing. Note the relationship of the interlobar fissures to the two horizontal planes. The practical significance of this arbitrary division of the pulmonary field is presented in the text and with the description of Figures 24 to 31.

Fig. 4. A right anterior oblique roentgenogram of the artificial chest shown in Figure 3.

placing lead foil between the pulmonary lobes *in situ*. This procedure proved to be none too satisfactory because only anteroposterior roentgenograms of the chest could be obtained. It was also found that the cooperation necessary to carry on such a study was difficult to obtain. Levitin and Brunn[3] carved model lobes of the lungs out of paraffin which offered little resistance to the passage of roentgen rays, bringing out the interlobar fissures by means of lead foil inserted between the lobes. These models were placed in position within the skeleton of a thorax and roentgenograms were obtained in various positions, such as posteroanterior, oblique and lateral. To illustrate the condition observed in the roentgenograms the authors resorted to diagrams as they did not consider the original roentgenograms satisfactory for reproduction. Such diagrams were none too satisfactory since the actual shape of the fissures and of the pulmonary lobes could not be appreciated due to the lack of an impression of depth in the diagrams. Peirce and Stocking[4] took roentgenograms of frozen sections of the thorax of cadavers which were cut in the right and left anterior oblique positions

and made careful comparisons between the roentgenograms and the corresponding section. These studies gave a fairly good idea of the lobes and fissures but they required reconstruction drawings to visualize the entire structures in these positions. In addition, the lungs in their specimens showed considerable disease and the thoraces were in a state of expiration so that the relationship to any bony landmark as seen in the usual roentgenogram would not be the same.

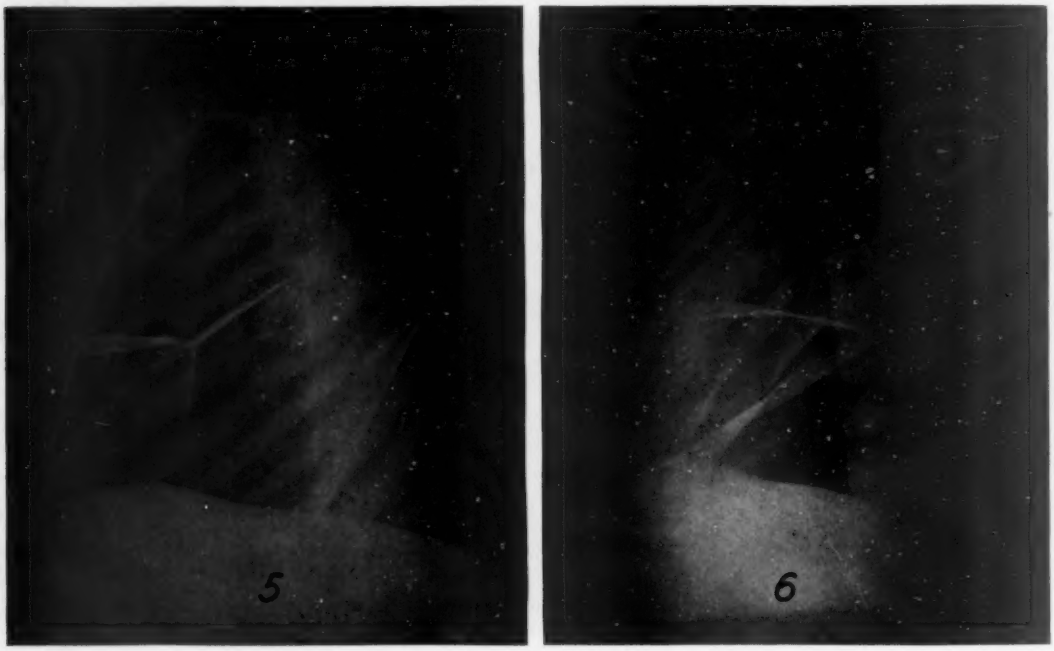


FIG. 5. A left anterior oblique roentgenogram of the same set-up as shown in Figure 3. Of particular interest is the considerable change in the configuration of the interlobar fissures when comparisons are made between Figures 3, 4 and 5.

FIG. 6. A left lateral roentgenogram of the model. This demonstrates clearly that the fissure between the right upper and middle lobes extends to the ventral but not to the dorsal costal surface. It is also to be noted that neither major fissure reaches to the ventral surface of the thoracic cavity while they both extend to the dorsal and to the diaphragm surfaces. The partial overlapping of the main fissures is plainly shown. This condition should be remembered when lateral roentgenograms of the human chest are interpreted.

It is practically impossible to obtain satisfactory molds or casts of entire lungs, or of lung lobes in the fresh state, because of the inherent nature of the tissue. For the same reason it is difficult to demonstrate the relationship of the interlobar fissures to the bony landmarks of the chest cavity, for normal lungs tend to contract to a certain extent when the thorax is opened, even in preserved cadavers. Any manipulation of the doughy tissue leads to artefacts which increase the difficulty of obtaining satisfactory roentgenograms in cadavers. The transference of entire lungs and of pulmonary lobes over to a solid substance that would permit of handling as one might choose would appear to be the procedure of choice in any study wherein anatomical relations are under consideration. It would also be desirable to use the same thorax from which the lungs are obtained but the acquisition of such a human thorax is next to impossible. No matter how such a study is carried out, artefacts cannot be avoided.

We conducted our study of this problem as follows: A pair of human lungs, free from

FIG. 7 and 8. A posteroanterior and a lateral roentgenogram of the right upper lobe covered with lead foil. The denser portions on the mediastinal and interlobar surfaces are due to several thicknesses of lead foil that the roentgen rays are obliged to penetrate and thus indicate the general contour of these surfaces. The notch in the upper portion of the lobe indicates the area occupied by the large vessels passing to the right arm and shoulder girdle. The diameter of the lobe is greatest in the dorsoventral axis and the interlobar surface has the shape of a check-mark with a short oblique dorsal and a long horizontal ventral portion.

FIG. 9 and 10. A posteroanterior and a lateral view of the right lower lobe. The mediastinal and diaphragmatic surfaces of this lobe are concave while the remainder of the outer surface is convex. The interlobar surface is twisted on itself and gives the appearance of a propeller blade when viewed laterally. The upper third is somewhat less perpendicular in its descent than the lower two-thirds. A considerable portion of the volume of this lobe lies below the highest level of the diaphragm. This area cannot be visualized in the posteroanterior view.

FIG. 11 and 12. A posteroanterior and a right lateral view with the right middle lobe and the main fissure covered with lead foil. This lobe has a wedge-like appearance when viewed from any angle. The mesial surface curves about the mediastinal contents in the ventral half of the chest. The volume of tissue ventral to the mediastinal contents as well as that portion resting upon the diaphragm is small. The dorsal tip of this lobe extends to about the mid-axillary line as is shown in the lateral view. The mediastinal surface is approximately of the same dimensions as the broadest lateral surface. The upper interlobar surface extends almost horizontally and is slightly convex. Lower interlobar surface is slightly concave and slightly twisted on itself to conform to corresponding portion of the lower lobe. Contact between the upper and lower lobes is dorsal and above the middle lobe.

FIG. 21. A posteroanterior view of an attempt to simulate a condition sometimes observed in roentgenograms of the chest. Note the wedge-shaped type of the "lesion" with the base in the lateral position. Such an appearance is commonly diagnosed as encapsulated interlobar effusion. Other views of this "lesion" are shown in Figures 22 and 23.

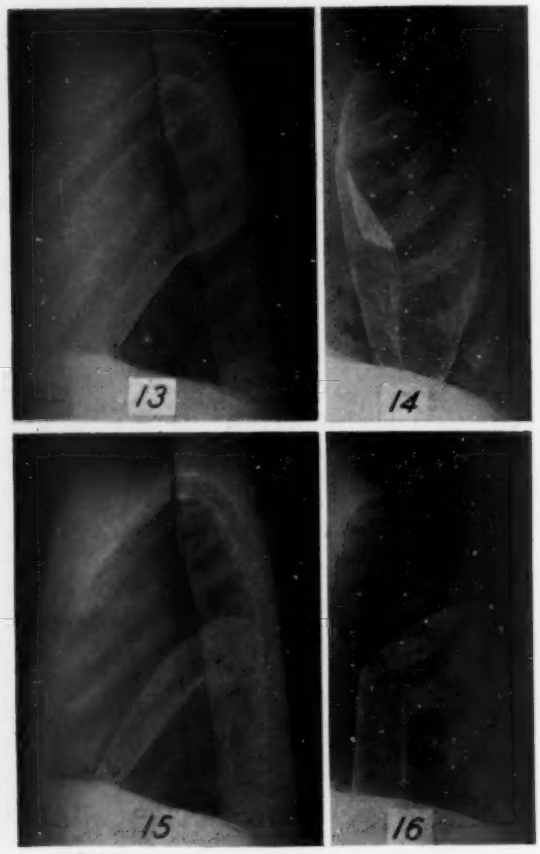


FIG. 13 and 14. These illustrate a left lateral and a posteroanterior roentgenogram of the left upper lobe. The greatest diameter of this lobe is vertical since it extends to the diaphragm although the volume of lung tissue is small at the diaphragm. The lobe extends around the mediastinal contents and is of small volume in the ventral flap. There is no cardiac notch, such as is usually described in textbooks of anatomy, in this particular specimen. The interlobar surface is slightly convex. About midway between the left anterior oblique and lateral positions this surface presents a linear appearance with a diagonal downward dorsoventral course of about 45 degrees.

FIG. 15 and 16. A left lateral and a posteroanterior view of the left lower lobe. The mediastinal and diaphragmatic surfaces are concave while the remainder of the outer surface is convex. A considerable volume of this lobe lies dorsal to the heart and is not seen in the usual posteroanterior roentgenogram of the chest. The same is true of smaller volume of tissue blocked out by the diaphragm. The interlobar surface is a reciprocal of the interlobar surface of the upper lobe.

macroscopic disease and with complete interlobar fissures on both sides, was obtained at necropsy.* This part of the program proved most difficult because of variations in the completeness of interlobar fissures and the presence of pleural or of interlobar adhesions. The lungs in the fresh state were moderately distended with 10 per cent formalin by the gravity method to approximate normal inspiration as nearly as one could judge with the lungs outside the thorax. In this condition they were immersed in 10 per cent formalin and thoroughly fixed for two weeks. The tissue was gradually dehydrated over a period of several months, starting with a 50 per cent solution of alcohol. The dehydrated lungs were placed in chloroform to displace the alcohol and later were transferred to a solution of chloroform saturated with paraffin. After several weeks in this solution the lungs were placed in melted paraffin in a paraffin oven, where many changes were necessary to get rid of the chloroform. The paraffin-impregnated lungs were then removed and quickly cooled to harden the paraffin. Because of the bulk of the tissue it took over a year to carry out the processes described. In the final process of hardening some irregular shrinkage of the lung surfaces, as well as of the entire lung, occurred since paraffin decreases in volume during the process of consolidation. These shrinkage defects were later remedied by molding modelling clay over the surface. During the whole procedure the interlobar fissures were not disturbed.

Plaster molds of each lung were made and master casts preserved. The lungs were then separated into lobes and molds and casts of each lobe obtained. Latex molds of the casts of the individual lobes were made and, by the use of these permanent molds, it is possible to obtain casts of any lobe as desired, either in plaster or paraffin. The master plaster casts of the whole lungs were placed in proper position and a plaster mold of the thorax was then cast with anterior, posterior and bottom portions. This was whittled down to crudely resemble the ex-

* We are indebted to Dr. J. Lebowich of the Saratoga County Laboratory for the pair of lungs we have used.

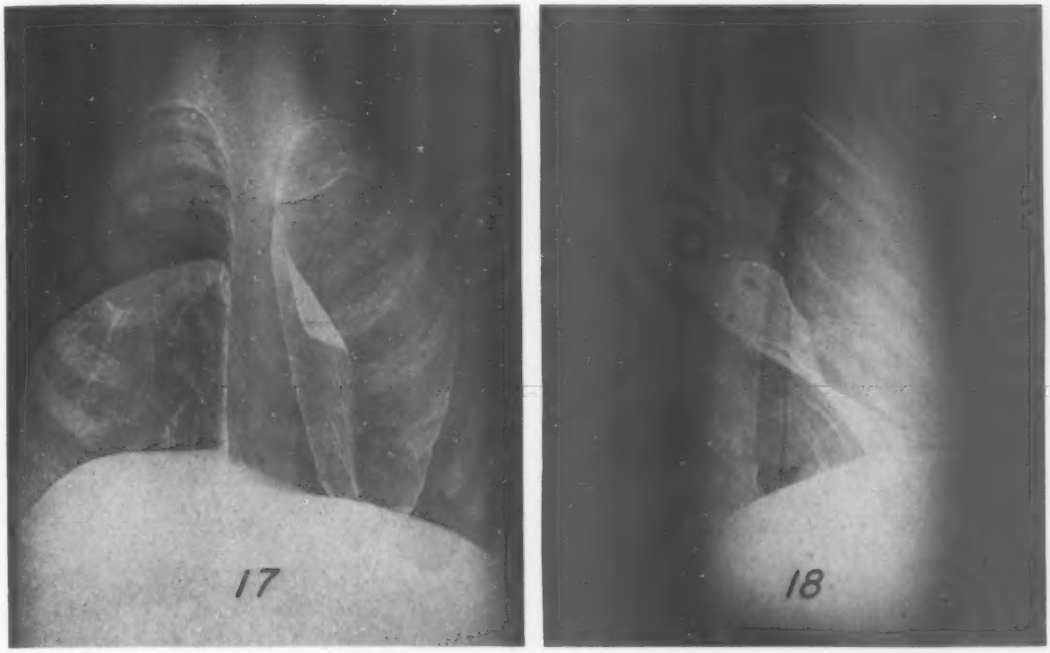


Fig. 17 and 18. A posteroanterior and a right lateral view with the right lower and left upper lobes covered with lead foil. Note the partial overlapping of the interlobar surfaces. The extent of this overlapping is shown more clearly in Figure 6.

Fig. 19 and 20. A posteroanterior and a left lateral roentgenogram with the right upper and left lower lobes covered with lead foil. Of particular interest is the partial overlapping of the interlobar surfaces as shown in the lateral view.

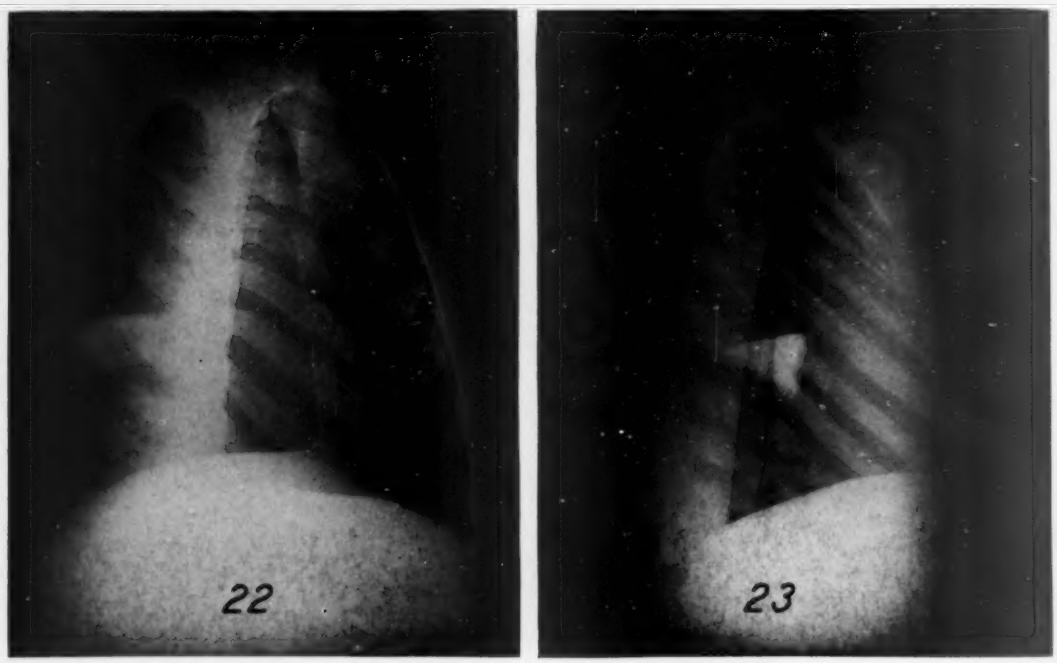


FIG. 22 and 23. A right antero-oblique (Fig. 22) and a right lateral (Fig. 23) roentgenogram of the same condition shown in Figure 21. In the oblique position the shape of the "lesion" has not altered but the change in the position demonstrates clearly that the area involved must be in the region of the dorsal portion of the middle lobe. The lateral view shows the complete involvement of the dorsal tip of the middle lobe instead of just the interlobar fissure. The purpose of this demonstration is to emphasize the fact that a localized pneumonia in this region can cast a shadow indistinguishable from an encapsulated interlobar effusion.

terior of the thorax. With the lung casts inside the mold of the thorax a cast of the mediastinal contents was obtained. A roentgenogram of the chest from a person corresponding in size and weight to the cadaver from which the lungs were obtained was placed interiorly over the anterior and posterior portions of the thorax mold and the position of the ribs was transferred. Since the roentgenogram used was taken at full inspiration it is probable that the lung fissures in the model are a trifle high in relation to the ribs, for the model was made from lungs judged to be in a position of normal breathing. The ribs were then painted on the inner surface of the artificial thoracic cage with white lead. With this variety of molds and casts it was possible to arrange any combination of conditions desired, and once the dummy was assembled roentgenograms could be obtained from any desired position in a manner similar to the taking of roentgenograms of the human thorax.

To demonstrate the position, size and shape of the interlobar fissures thin sheets of lead foil were placed between the lobes, and to accentuate the size and position of the lobes and of the mediastinal contents the visceral pleural surfaces of these structures were covered with thin lead foil. Pathological processes known to exist in human lungs could be simulated by using substances of greater or lesser resistance to roentgen rays than the remainder of the lung casts would possess, thus controlling gradations in density. While it is admitted that this type of model contains a good deal of artificiality, it is possible to prepare an "artificial set-up" and to test the ability of the roentgenologist to accurately interpret the size, shape and location of "lesions" placed at will within the casts of the lungs. Likewise, such a procedure can serve

to assess the accuracy of serial sections by planigraphy.

The size and exact shape of the lungs and of the thorax may not be entirely correct, but they are well within the range of variations that are encountered in human thoraces. The position and contour of the interlobar fissures are correct for the pair of lungs used. The absence of the structures exterior to the chest cavity, of the heart and other tissues of the mediastinum, of the bronchial tree, and of the normal lung "markings" is to be regretted, but it helps to emphasize the position, site and size of such things as the interlobar fissures, the lobes of the lungs and the mediastinal contents.

The main interest to those who are concerned with the interpretation of pulmonary shadows as seen in roentgenograms is, of course, the illustrations which accompany this paper. They are all prints reduced from the actual roentgenograms of the model which were taken on the usual 14×17 inch film. The roentgenograms were taken at a distance of 5 feet from the object with a technique found by trial to give a penetration that would clearly demon-

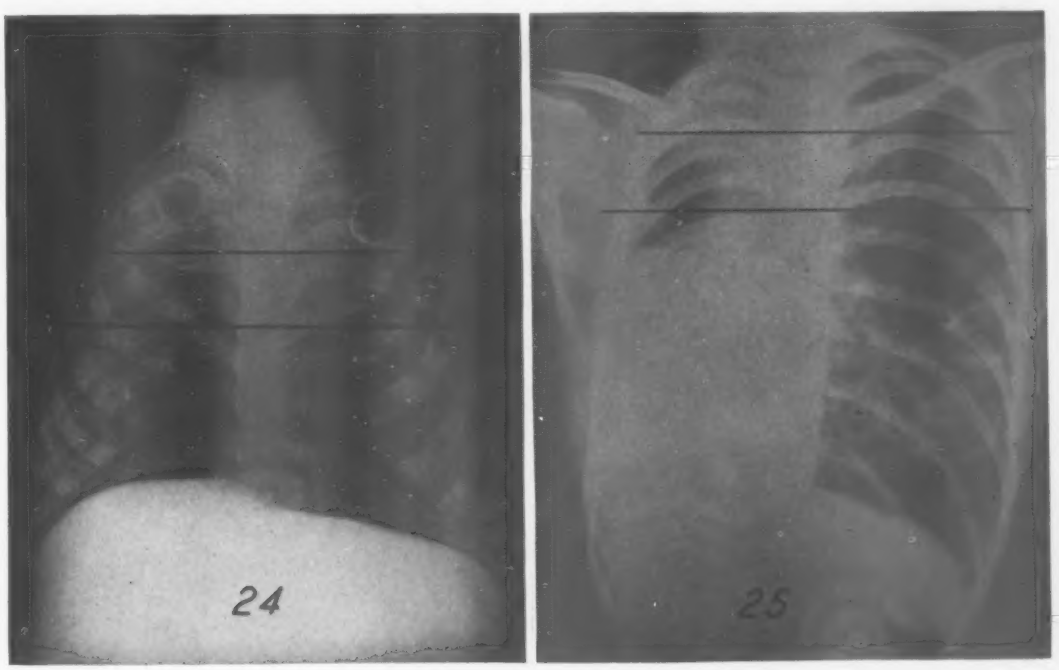


Fig. 24. A posteroanterior roentgenogram with simulated tuberculous cavities placed in the various lobes of the lungs in locations where such lesions are commonly encountered in each lobe. These cavities may vary in their location in all directions but they are preponderantly in the upper portions of each lobe. Since the interlobar fissures are not visible it is not possible to state the location of the three lower cavities with respect to the lobe involved. The horizontal planes, represented by lines, are drawn at the level of the fourth and sixth costovertebral junctions. To appreciate the relation of the interlobar fissures to these lines refer back to Figure 3. A lateral view would show that all but the lowest cavity on the right were located dorsally.

Fig. 25. A posteroanterior roentgenogram of proved tuberculosis taken one year before death. The considerable displacement of the tissue to the right caused the development of an emphysematous left lung. With such a condition a downward displacement of the interlobar fissure would be anticipated. Since the cavity on the left is below the plane drawn at the level of the sixth costovertebral junction and was known to be dorsal in position the location could be stated to be in the upper portion of the left lower lobe. Necropsy revealed a markedly emphysematous lung with a thin-walled cavity in the lateral area of the upper portion of the lower lobe with the upper edge of the cavity 2.5 cm. below the apex of the lobe.

strate the structures within the "dummy." The reader is asked to overlook the aberrant shadows in the roentgenograms and to consider only the main features portrayed, for we admit considerable ineptitude in the artistic handling of the subject matter. The descriptions of the roentgenograms accompany the illustrations.

DISCUSSION

In presenting the studies we have conducted, our main purpose is to give to those concerned with the interpretation and treatment of pulmonary disease a clear and useful concept of the anatomical relationship of the pulmonary lobes and of the interlobar fissures to the bony landmarks as seen in roentgenograms of the chest. The usual posteroanterior, oblique and lateral positions have been illustrated and stereoroentgenograms would have been added had the expense of illustration not been prohibitive. It is hoped that the illustrations reproduced will convey the three dimensional structures of the chest.

It is fully realized that the exact relation-

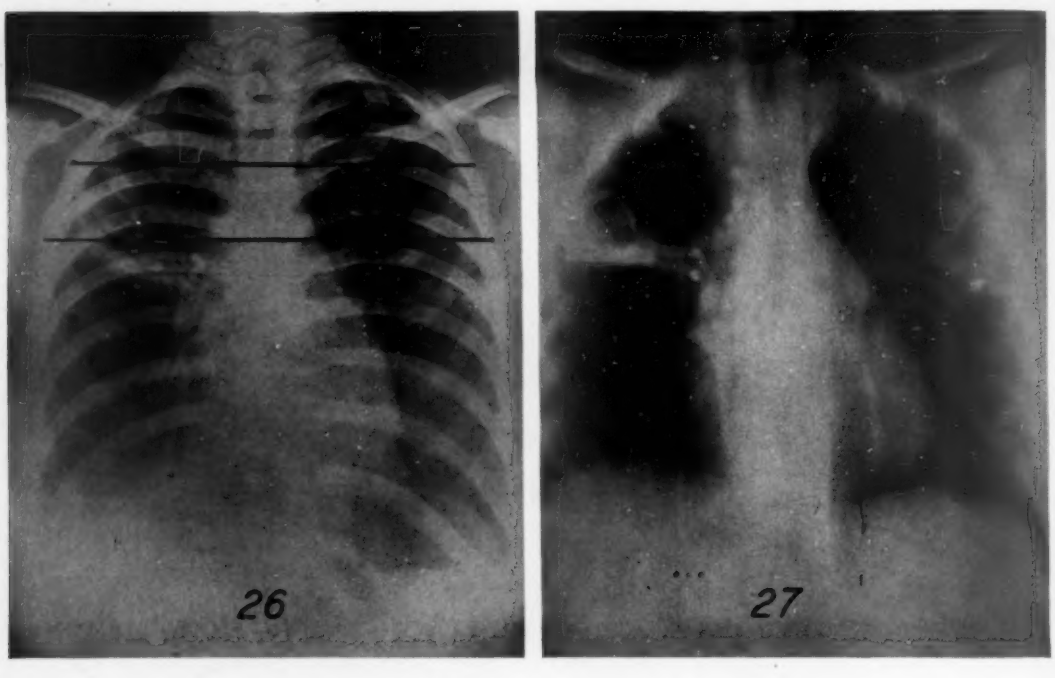


FIG. 26. A posteroanterior roentgenogram of a proved tuberculous case taken about one year before death. There is a pathologic process between the two planes on both sides with a definite cavity cut across by the lower plane on the right. Without the dorsoventral location of the lesion it is impossible to define the lobe involved. Fig. 27. A planigram taken 9 cm. from the table top showing the sharpest outline of the cavity on the right. The lesion on this side was evident at 5 cm. so that it was distinctly dorsal in position. The lesion on the left became evident at 9 cm. and a multilocular cavity was shown ventral to this section. Applying the knowledge gained from studies of the dummy it can be stated that the lesion on the right is in the apical portion of the lower lobe and, on the left, in the upper lobe ventral to the upper portion of the lower lobe. These deductions were proved correct at necropsy. On the right, dense adhesions were present over the area involved and this condition undoubtedly displaced the lesion somewhat upward and laterally. This displacement was not sufficient, however, to invalidate the deductions made. From the lower shelf-like edge shown in Figure 27 one might be led to believe that this represented the interlobar fissure and since the cavity lies above the shelf the pathologic process must be in the upper lobe. Necropsy showed very little involvement of the interlobar fissure while the entire apical portion of the lower lobe was involved. The dense area seen simply represents parenchymal tuberculosis. The course of the interlobar fissure in this region is such that a broad plaque rather than a shelf-like appearance would be expected if the fissure was involved to a degree sufficient to cast a shadow.

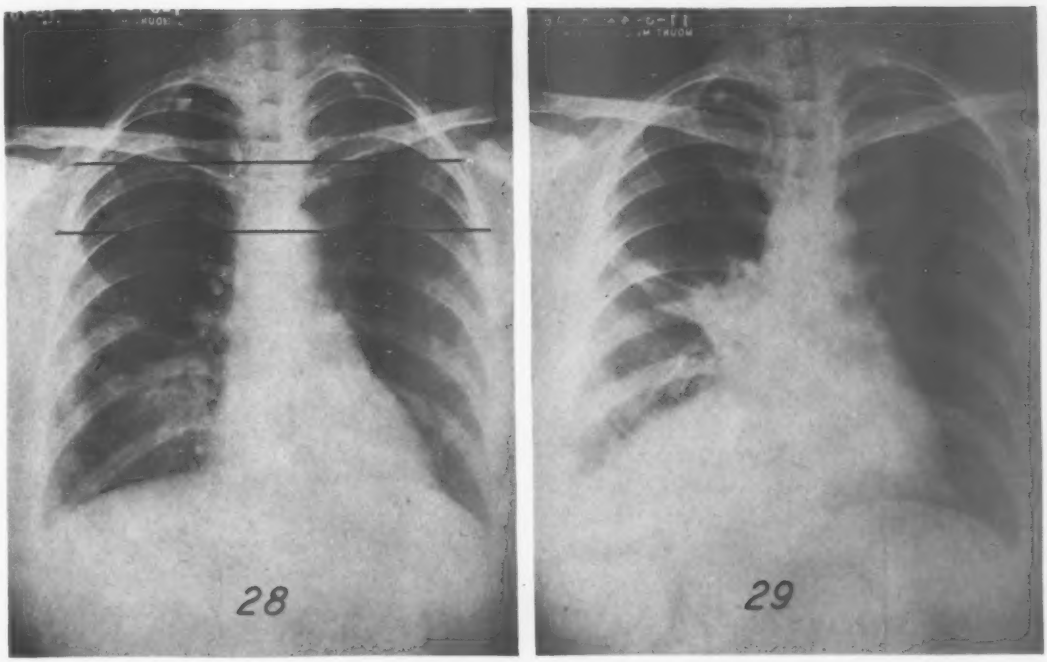


Fig. 28. A posteroanterior roentgenogram of a tuberculous case showing a pathologic process below the lower plane with a definite cavity on the right between the two arrows. This lesion was definitely ventral in position and a diagnosis of middle lobe tuberculosis was made and substantiated when a lobectomy was performed. The tuberculous involvement was found to be in the upper portion of the lobe. Note that the lowest cavity on the right in Figure 24 is similar in position to the cavity present in this case. Fig. 29. A posteroanterior roentgenogram of the same individual three months after operation. This shows the absence of the lesion demonstrated in Figure 28.

ship of the large anatomical units of the lungs to the ribs is not constant, for in both inspiration and expiration the movement of the bony cage and of the pulmonary tissue is in opposite direction. Local pleural adhesions, atelectasis, emphysema, and consolidation of tissue as in pneumonia, also affect this relationship to some extent. An anomaly such as a single lobe in the left lung, for instance, would invalidate any interpretation on the left side. We believe, however, that the relationships observed in the artificial thorax are applicable to interpretations of the average human chest provided there is no undue distortion caused by a considerable amount of pulmonary disease. A practical application of the knowledge gained from studies of roentgenograms of the artificial thorax has been made on 3 cases in which the site of tuberculous cavities was in the less common location and in which proof of the anatomical location was available from necropsy or surgical reports. The deductions made from roentgenograms taken several months prior to necropsy or surgical reports were found to be valid in spite of distortions caused by the pathological condition present at the time the roentgenograms were taken. Horizontal planes through the chest at the level of the fourth and sixth costovertebral junctions have a practical value when interpretations in relation to pulmonary lobes are under consideration. The costovertebral junctions were selected because they are stationary and because the relationship of the lobes and interlobar fissures to the costovertebral junction changes much less than it does to the ventral portions of the ribs during the process of respiration. The practical value of interpretations of chest roentgenograms will be

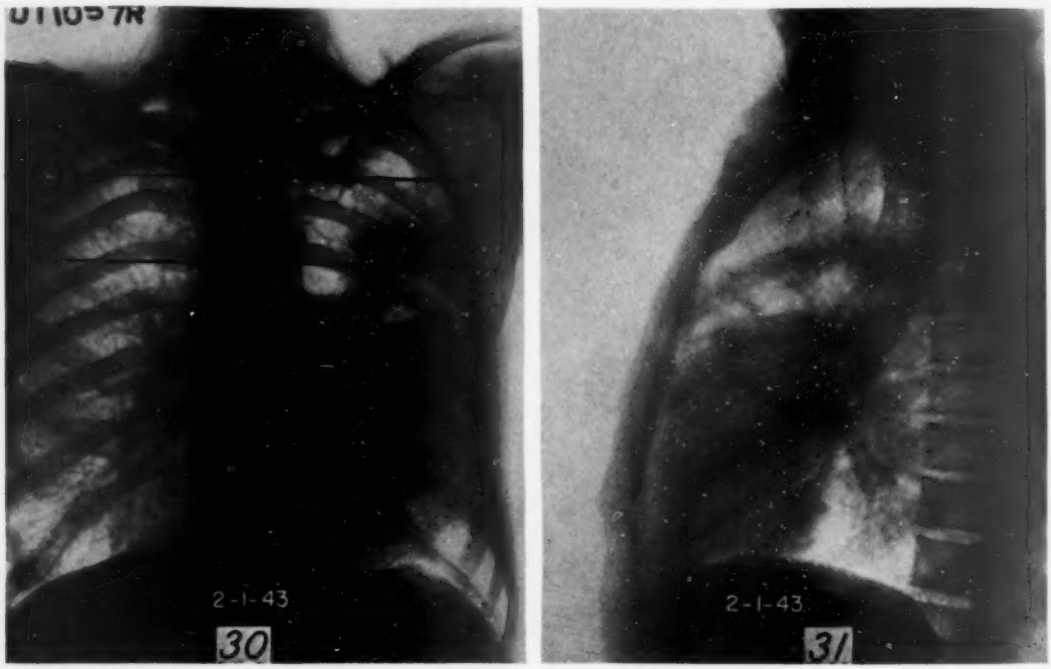


FIG. 30 and 31. A posteroanterior and a left lateral roentgenogram, respectively, from a case kindly lent by Dr. J. Burns Amberson of Bellevue Hospital, New York City. The patient was a white male, aged fifty-five, who had had a chill with accompanying cough and continuous sharp pain in the upper anterior portion of his left chest five days previous to hospitalization. A diagnosis of pneumonia was made. Within a few days it became evident that a necrotizing process was present and that a sequestrum of lung was forming. These roentgenograms were taken shortly before surgery was resorted to. At operation a sequestrum the size of a lemon was found in the mid-portion of the left upper lobe, with the pathologic process limited to this lobe. The patient made satisfactory progress following operation.

The illustrations are given to demonstrate how a pathologic process limited to one lobe may indicate the position of an interlobar fissure. That the upper lobe is involved is suggested in Figure 30 from the triangular clear zone resting on the diaphragm (refer to Fig. 3). The lateral view not only confirms the upper lobe involvement but also indicates the position of the interlobar fissure by the sharp limitation of the lesion. That only the upper half of the fissure is outlined can be surmised from a comparison with Figure 13. It is doubtful if the lower ventral angulation of the dark shadow represents the course of the fissure. The presence of a sequestrum is strongly indicated in the lateral roentgenogram.

Horizontal planes through the chest at the level of the fourth and the sixth costovertebral junctions show that a pathologic process is present in this region and that an apical involvement of the lower left lobe has to be ruled out. The lateral view shows a normal apex of the lower lobe and the lesion in the upper lobe, ventral to the lower lobe. The position of the left interlobar fissure corresponds closely to the position shown in the artificial thorax (Fig. 13.)

enhanced provided the following suggestions in relation to the two planes just mentioned are used:

1. Pathologic processes above a horizontal plane at the level of the fourth costovertebral junction will be in the upper portions of the upper lobes. In tuberculosis the majority of lesions will be dorsal in position.

2. Below a horizontal plane at the level of the sixth costovertebral junction pathologic processes in the dorsal half of the chest will be in the lower lobes, especially if the main lesion abuts the dorsal surface of the chest cavity. Pathologic processes in the ventral half will be in the upper lobe on the left and in the middle lobe on the right.

3. The area between horizontal planes at the fourth and sixth costovertebral junctions represents the common variations of the upper edge of the main fissures on either side. In the pair of lungs we have used the upper edge of these fissures is about median in position and probably represents the average. If in this area the pathologic condition is present in the ventral two-thirds of the chest the upper lobes are surely involved. If, however, the lesion adjoins the dorsal surface, involvement of the apex of the lower lobe must be seriously considered. To determine which lobe may be involved pleural endoscopy may have to be employed, especially if the lesion lies in the upper portion of this area.

It is our hope that the data presented may prove to be of practical value to all who are concerned with the interpretations of roentgenograms of the chest and with the treatment of pulmonary disease.

REFERENCES

1. Sampson, H. L., Heise, F. H., and Brown, L. Study of pulmonary and pleural annular radiographic shadows. *Am. Rev. Tuberc.*, 1918–1919, *2*, 664–689.

2. Berry, F. B., and Childs, E. P. Fissures of the lungs. *Ann. Surg.*, 1932, *96*, 961-972.

3. Levitin, J., and Brunn, H. Study of roentgenologic appearance of lobes of lung and interlobar fissures. *Radiology*, 1935, *25*, 651–680.

4. Peirce, C. B., and Stocking, B. W. Oblique projection of the thorax; anatomic and roentgenologic study. Am. J. Roentgenol. & Rad. Therapy, 1937, *38*, 245–267.

THE ROENTGENOGRAPHIC MANIFESTATIONS OF ATYPICAL PNEUMONIA OF UNKNOWN ETIOLOGY

By W. E. CRYSLER, M.D., D. Rad.*
A/Surgeon Lieutenant Commander
ROYAL CANADIAN NAVAL VOLUNTEER RESERVE

DURING the past decade a moderately infectious constitutional disease with frequent evidence of atypical pneumonia has been increasingly recognized and reported. Dingle and Finland[3] have contributed the most exhaustive recent review of the subject. They state that the condition was recognized clinically as long ago as 1872, and a pathological process was described at about that time. It seems likely that the disease was prevalent before the pandemic of influenza in 1918 and that it existed in the military forces, where it was given such names as "catarrhal fever" and "soldier's pneumonia."

The increased use of roentgenological examination in the diagnosis of inflammatory diseases of the respiratory tract has shown that a variety of roentgenological opacities in the lung fields, often transitory, may occur in the course of such diseases without the grave symptoms associated with the generally recognized forms of pneumonia.[6]

The condition has been graced with numerous terms, the multiplicity of which is due to various investigators' conception of the disease in which the clinical, laboratory and roentgen findings do not follow a definite and clear-cut picture. It has been variously referred to as virus pneumonia, acute influenzal pneumonia, acute pneumonitis, acute interstitial pneumonitis, pneumonitis, atypical pneumonia with leukopenia, current bronchopneumonia of unusual character and undetermined etiology, bronchopneumonia of unknown etiology. Clinically it is probably best termed "primary atypical pneumonia, etiology unknown."[3]

From a roentgenologic standpoint, only an anatomical diagnosis can be given in cases of pneumonia, e.g., "pneumonia of lobar distribution" or "pneumonia of lobular or segmental distribution." Ramsay and Scadding[6] have pointed out that, in order to make a complete diagnosis, both the etiological and anatomical terms must be included in the description of a pneumonia; for example, "pneumococcus type 1 right lower lobar pneumonia" is a specific diagnosis.

According to the roentgenographic shadows produced by the pulmonary lesions, several have reported findings which on analysis of illustrations and descriptions seem to be, for the most part, similar, if not identical.

Seeds and Mazer[10] thus segregate the lesions into three main groups, viz.: "cotton wool," "pseudofibrosis," "wire glass." While these terms are useful in describing a given lesion, they should not be used in identifying a type of pneumonia.

Bowen[2] has reported a group of cases occurring among soldiers in Honolulu and he points out the similarity in roentgenographic appearance to such conditions as pulmonary tuberculosis, lung abscess, acute bronchiectasis, bronchogenic carcinoma and metastatic carcinoma.

Ackermann[1] has also drawn attention to the resemblance of certain cases to pulmonary tuberculosis. However, Ramsay and Scadding state that the roentgenogram is never sufficiently characteristic to justify a dogmatic diagnosis of pulmonary tuberculosis without supportive evidence and without a period of observation.

Kornblum and Reimann[4] have studied a group of cases occurring among medical students, interns and nurses on whom roentgenograms of the chest were obtained at frequent intervals during a mild epi-

* Formerly Resident in Radiology, Department of Radiology, Toronto General Hospital and University of Toronto.

demic of atypical pneumonia. They describe the picture of "acute tracheobronchitis" which they believe represents an early stage of this infectious process. While they recognize the difficulty in making such a diagnosis, they state that the process causes increase in density and size of the hilum and trunk shadows which are ill defined and distinctly blurred, with occasional mottling of the pulmonary tissues about the hilar area. They attach considerable importance to a generalized haziness found throughout the lung field which they consider due to acute congestion of the interstitial blood vessels.

The observations of Ramsay and Scadding suggest that the association of lobar atelectasis with catarrhal infections of the respiratory tract producing no special acute symptoms is more frequent than is commonly recognized. Their report includes 4 cases in which there was evidence of lobar atelectasis and 21 cases of pneumonia. Reimann's[7] Case 9 showed evidence of basal atelectasis. Scadding[8,9] in further reports classifies the pneumonic lesions in two main groups, viz., "benign circumscribed pneumonia" and "disseminated focal pneumonia." The benign circumscribed variety he describes as a fairly well localized, but not sharply defined lesion of uniform density, located usually in the lower lobes. The disseminated focal type produces the roentgenological picture of diffuse, rather coarse mottling in foci varying from 2 to 5 mm. in diameter. He[8] classifies his cases into those with constitutional symptoms but without clinical or roentgen evidence of pneumonia; those with clinical localizing signs (suppressed breathing and fine moist râles), and finally those with both clinical and roentgen localizing signs. He observed a definite lag of two to three days between clinical and roentgen localizing signs.

Briefly, the condition is recognized clinically by fever, cough, malaise, headache, chilliness. Sputum when present is usually mucopurulent, occasionally blood streaked, and rarely frank blood. The physical findings include pharyngeal injection; some cases show prostration and rarely dyspnea with cyanosis. Early pulmonary signs, if present, are limited to fine or medium moist râles with slight dullness. Later, as resolution occurs, loud râles and rhonchi are heard. The leukocyte count is either slightly elevated, normal or slightly depressed. The sedimentation rate may be elevated. The sulfonamides are ineffectual. Complications are few.

Etiology. Dingle and Finland state that the etiology of atypical pneumonia has not been established satisfactorily. The above clinical syndrome may be produced by a number of known bacteria and viruses, and yet in the majority of outbreaks, in which studies were made, none of these agents were identified with the disease.

Kornblum and Reimann hold the same view and remark that the similarity of this disease to other infections of the lungs gave rise to the thought that their epidemic was due to a filterable virus.

Pathology. Cases coming to necropsy are few. According to Dingle and Finland, the chief pathological features of fatal cases reported by Kneeland and Smetena and by Longcope are those of a patchy, hemorrhagic interstitial pneumonia associated with acute bronchitis and bronchiolitis. Grossly there are areas of atelectasis and emphysema, small areas of red or gray consolidation, which in some places appear to have become confluent. The bronchi are filled with mucoid or purulent exudate. The microscopic findings include hemorrhagic or mononuclear alveolar exudate and infiltration of alveolar septa with mononuclear cells; the septa may later show thickening with reduction of the alveolar spaces. The walls of the bronchi and trachea show necrosis and infiltration with polymorphonuclear cells.

REPORT OF CASES

This report is based on 178 cases of bronchopneumonia, demonstrated by roentgenographic examination, occurring in personnel of the Royal Canadian Navy who were referred with clinical features con-

forming to those described. Bacteriological studies, when done, revealed no positive pathogens. This group had, as do all R.C.N. personnel, routine chest roentgenograms on entry.

Method. As a routine, posteroanterior and the appropriate lateral roentgenograms of the chest are obtained either at the bedside or in the roentgenographic department, depending on the condition of the patient. The majority of cases in this group include admission and progress roentgenograms. A case is not released from the hospital until the chest roentgenogram shows complete clearing of the process.

ROENTGENOGRAPHIC FINDINGS

There is no notable relationship between the anatomical extent of the disease as shown in the roentgenogram and the severity of the symptoms. Pneumonic infiltrations have been discovered in the enlistment roentgenograms of 12 recruits who have had no complaints other than a recent "chest cold." The appearance and anatomical extent of these infiltrations are identical with those of individuals in the hospital who were considered too sick to be transported to and from the department and on whom roentgenograms secured at the bedside were necessary. A lag of two to three days has occasionally been noted between the clinical and roentgen evidence of pneumonia.

TABLE I

FREQUENCY OF LOCATION OF PNEUMONIC INFILTRATIONS

	per cent
Left lower lobe	44
Right lower lobe	35
Right upper lobe	7
Accessory right lower lobe	4
Left hilar	4
Right hilar	2
Left upper lobe	2
Right middle lobe	2

Location. The frequency of involvement of the various lobes is given in Table 1. One hundred and eighty-one lobes were involved in 178 cases. Eighty per cent of lesions were confined to the lower lobes.

Roentgenographic Appearance. In almost all cases, the parenchymal infiltration manifests itself by a peribronchial distribution, viz., bronchopneumonia. While a lesion in the posteroanterior projection may appear of lobar distribution, nearly always the lateral projection reveals the process to be a segmental, confluent bronchopneumonia, radiating in a fanwise manner from the hilum. It is true that an infiltration of lobar distribution is occasionally demonstrated in a case with a clinical picture conforming to that described.

Early infiltration commences in one of two ways:

First, an ill defined, blurred, localized structural accentuation occurs. If the disease progresses anatomically, the peribronchial blurring extends and coalesces, producing a frank parenchymal infiltration (Fig. 1). This varies in density from a slightly impaired translucency to a ground glass appearance and occasionally progresses to a moderate density, but rarely equals that of the cardiac shadow unless complicated by pleuritis (Fig. 2). An infiltration of moderate density may be visualized, for example, in the posteroanterior view, but this has been shown to be almost always transparent in the lateral projection. Accentuated structural markings are usually visible through this density and appear prominent.

The second method of development is first manifested by an area of localized, rather dense structural accentuation. If the anatomical extent progresses, flocculent densities, peribronchial in distribution, appear (Fig. 3).

Finally, occasionally both homogeneous and flocculent densities are demonstrated in the same lesion, thereby resulting in a homogeneous lesion through which "double densities" are visualized which merge imperceptibly into the adjacent infiltration.

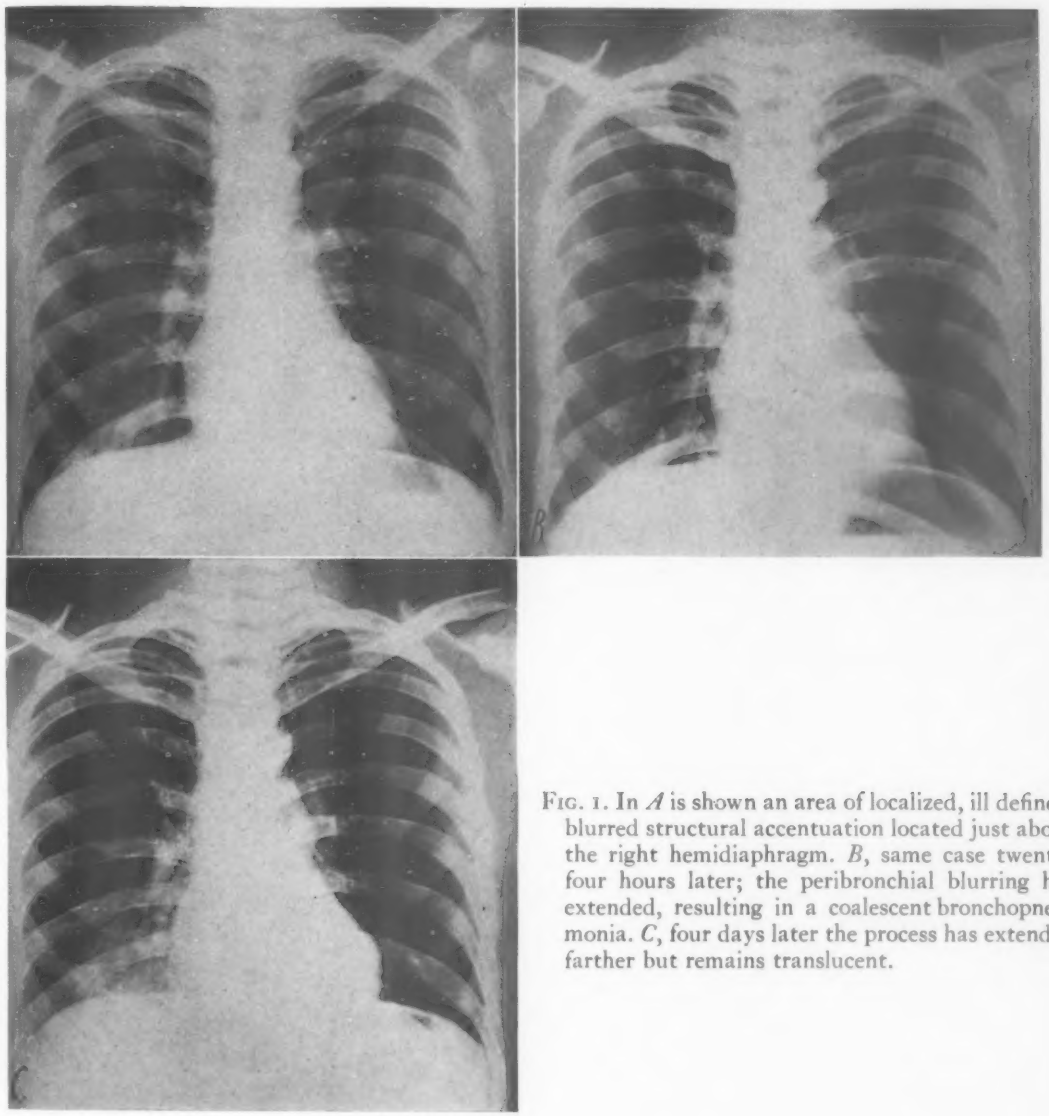


Fig. 1. In *A* is shown an area of localized, ill defined, blurred structural accentuation located just above the right hemidiaphragm. *B*, same case twenty-four hours later; the peribronchial blurring has extended, resulting in a coalescent bronchopneumonia. *C*, four days later the process has extended farther but remains translucent.

To summarize:

A. *Homogeneous Group:*

1. The purely homogeneous lesion as described above.

2. The ill defined and blurred structural accentuation—probably an early manifestation.

3. The "cotton wool" lesion, composed of several adjacent homogeneous circular lesions which do not coalesce.

B. *Flocculent Group:*

1. The purely flocculent and rather dense lesion.

2. The dense linear accentuation—probably an early manifestation.

3. Linear accentuation with occasional areas of dense flocculent infiltration.

C. *Homogeneous Flocculent Group:*

The frequency of these various types has been analyzed and is given in Table II.

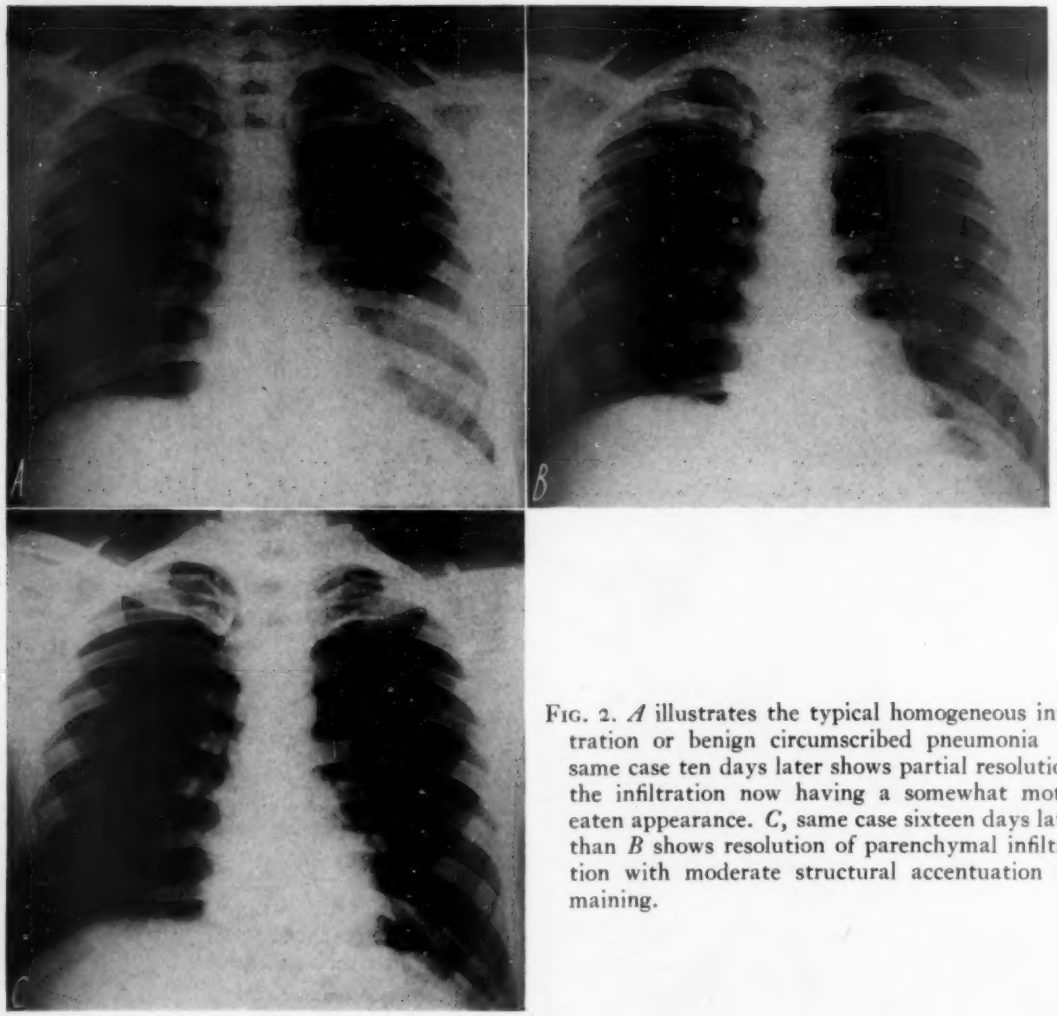


FIG. 2. *A* illustrates the typical homogeneous infiltration or benign circumscribed pneumonia *B*, same case ten days later shows partial resolution, the infiltration now having a somewhat moth-eaten appearance. *C*, same case sixteen days later than *B* shows resolution of parenchymal infiltration with moderate structural accentuation remaining.

Hilar adenopathy, increase in density of the hilum, ill defined accentuation of the trunk shadows with obliteration of the translucent space between the inner border of the right hilum and the right border of the heart have been demonstrated in a number of basal infiltrations.

Resolution in the homogeneous group is revealed by a reduction in total density at which time the infiltration assumes a moth-

TABLE II

FREQUENCY OF THE TYPES OF ROENTGENOGRAPHIC DENSITIES

Homogeneous	Homogeneous with Structural Accentuation	Cotton Wool	Flocculent	Flocculent with Structural Accentuation	Dense Structural Accentuation	Homogeneous Flocculent
30.8%	12.3%	3.3%	20.7%	12.3%	6.7%	13.9%
46.4%			39.7%			13.9%

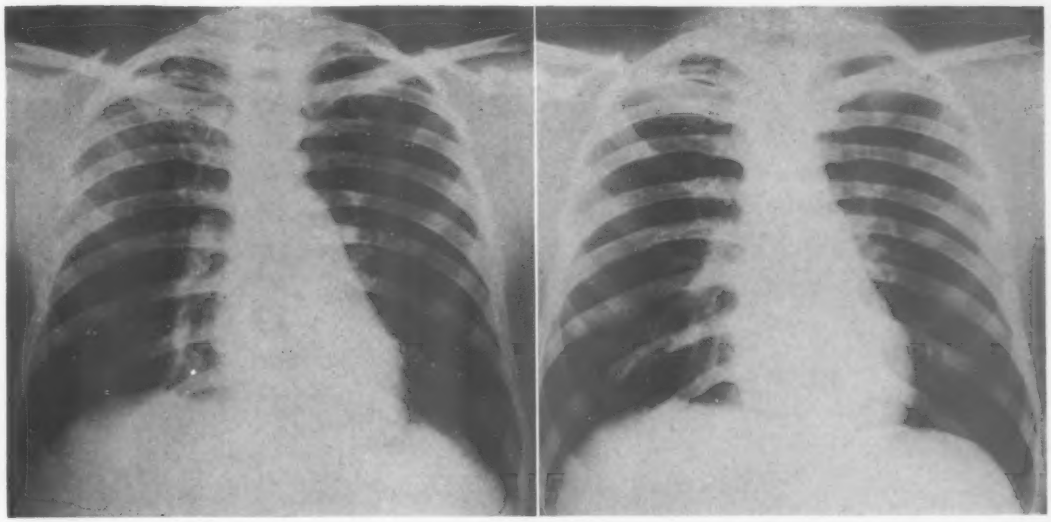


Fig. 3. *A*, an example of the flocculent or disseminated focal infiltration occurring at the right apex, resembling pulmonary tuberculosis; parenchymal infiltration is also demonstrated at the right cardiohepatic angle. *B*, same case eighteen days later showing complete resolution.

eaten appearance. When regression of the infiltration is complete, the structural accentuation often recedes more slowly and is last to disappear. The flocculent lesions and associated structural accentuation resolve more or less together, becoming gradually less dense (Fig. 2).

Certain lesions of either homogeneous or flocculent type, when confined to the upper lung field, resemble pulmonary tuberculosis. Re-check examination in two weeks usually allows a definite opinion (Fig. 3).

Pleuritis with effusion as recognized on the roentgenogram is a rare finding. Evi-

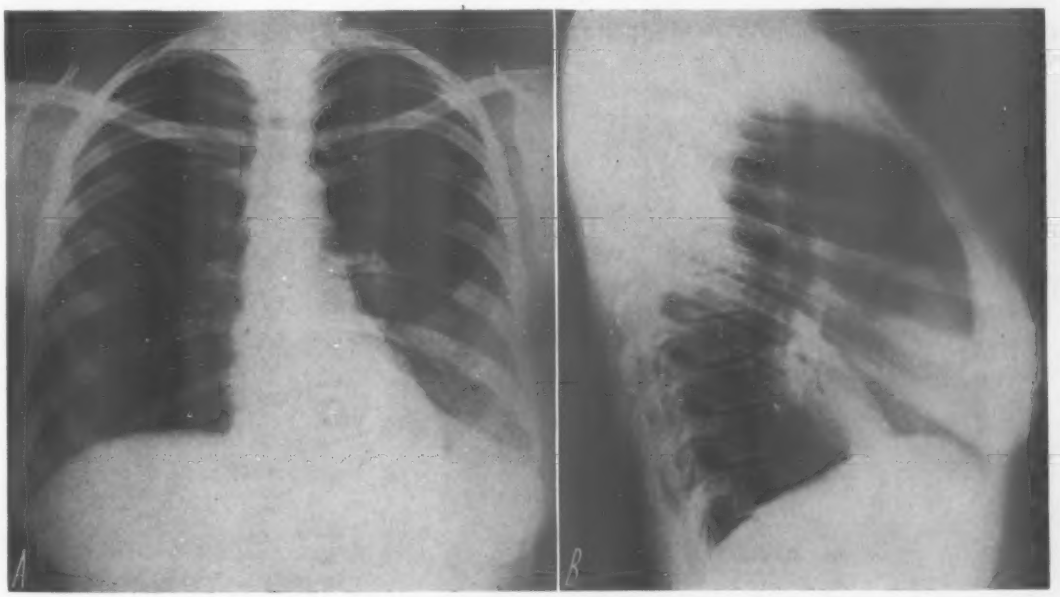


Fig. 4. *A* and *B*, interlobar pleuritis with effusion located at the lower end of the left fissure. Note the similarity between 4*A*, 1*C* and 2*A*; the lateral roentgenogram makes an accurate differentiation.

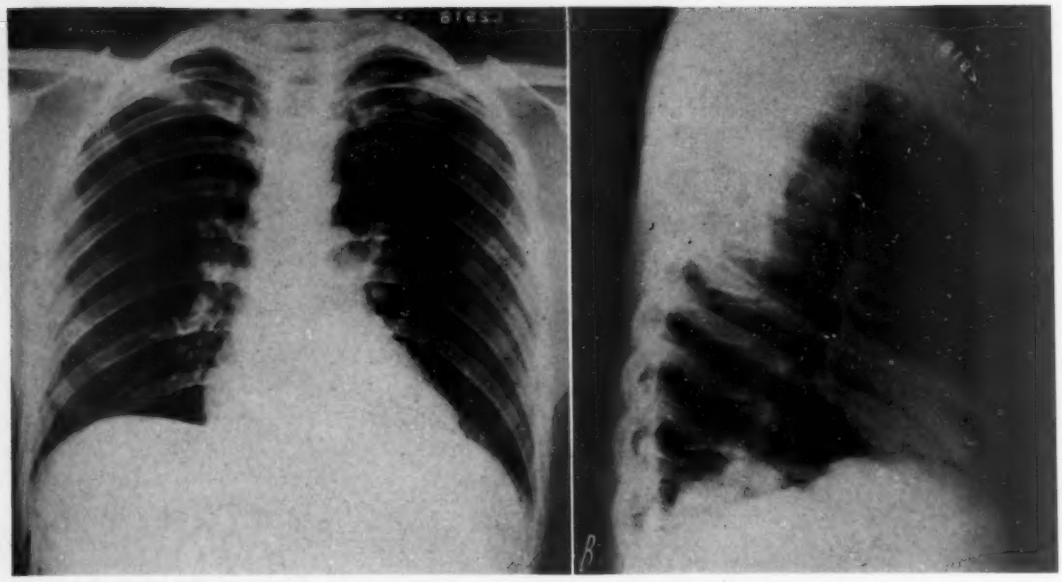


Fig. 5. *A*, portable anteroposterior roentgenogram shows no evidence of parenchymal infiltration, but slight elevation of left hemidiaphragm is present. *B*, the left lateral roentgenogram clearly demonstrates a triangular density radiating downward in a fanwise manner from the left hilum and is confined to the left lower lobe, thus localizing the process behind the heart.

dence of coexistent interlobar or parietovisceral pleural thickening was observed in 22 cases and then only when the parenchymal process was adjacent to the pleura.

The homogeneous density of parenchymal infiltration is similar in appearance in many cases to that of interlobar pleuritis. As described and illustrated by Levitin and Brum,[5] the lateral projection has served to make an accurate differentiation (Fig. 4).

The lateral projection was used in 100 cases in this series. In 25 of these, it was of no assistance; in 71 the appropriate lateral roentgenogram not only localized the process, but provided an insight into the actual area of parenchyma involved. In 3 cases the process was demonstrated either below the summit of the dome or behind the heart and in none of these was the process recognized in the posteroanterior projection (Fig. 5 and 6).

Elevation of a Hemidiaphragm. This finding has been noted in a total of 38 cases, or 21.3 per cent, and has been interpreted as evidence of atelectasis (Fig. 7). This has varied from slight to marked elevation;

Table III

Length of Time for Anatomical Resolution*

Type of Lesion	No. of Cases	Average No. of Days
Homogeneous infiltration	52	16.0
Flocculent infiltration	46	15.4
Combined infiltration	9	13.7
Slight elevation of hemidiaphragm	13	14.6
Moderate and marked elevation of hemidiaphragm	7	17.4

* A total of 142 cases had serial examinations of which 127 are included in Table III and 15 in Table IV.

Table IV

Cases Discharged as Clinically Resolved and in Which Anatomical Resolution Was Not Entirely Complete

Lesion	No. of Cases	Average No. of Days
Residual structural accentuation	8	23.5
Residual elevation of hemidiaphragm with or without residual structural accentuation	7	33.5

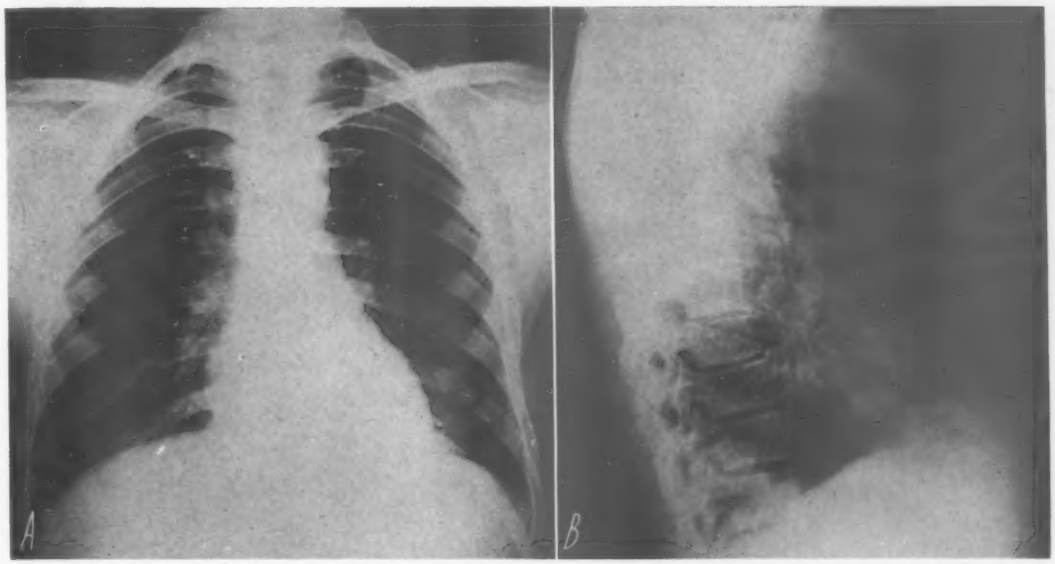


Fig. 6. *A*, posteroanterior roentgenogram shows no evidence of parenchymal infiltration. *B*, right lateral projection (reversed) demonstrates an area of parenchymal infiltration located in the right lower lobe at its posterior costophrenic angle below the summit of the right hemidiaphragm.

Fleischner's lines have also been noted. Only rarely are other signs of atelectasis observed, e.g., mediastinal displacement, narrowing of rib spacing.

As noted in Table III, atelectasis as a coexistent finding results in a prolongation of resolution.

Complications. As shown in Table III, anatomical resolution occurs in approximately two weeks. This is occasionally prolonged, as Table IV shows, but these cases have been clinically clear. Not included in Table IV are 5 cases of non-resolution which developed complications.

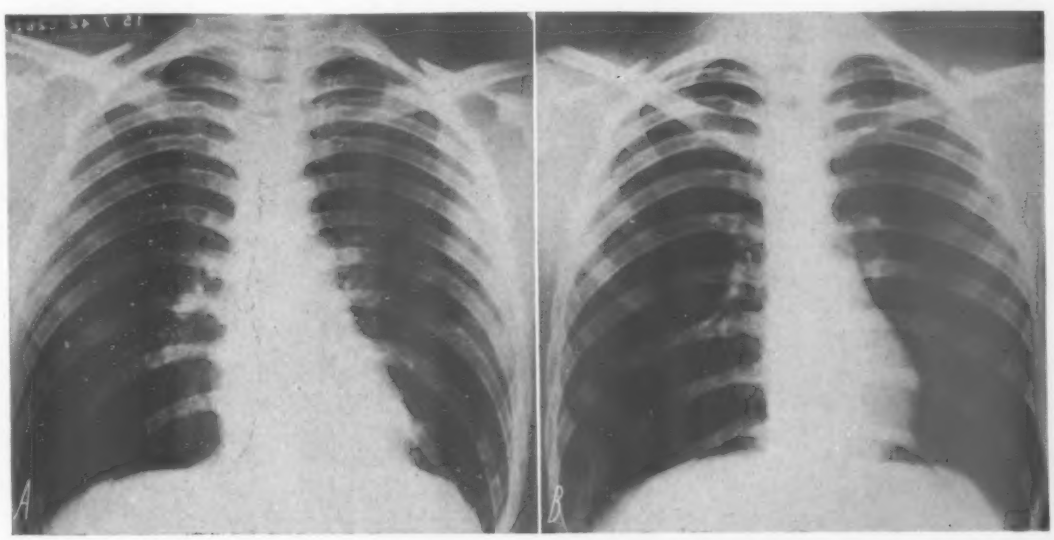
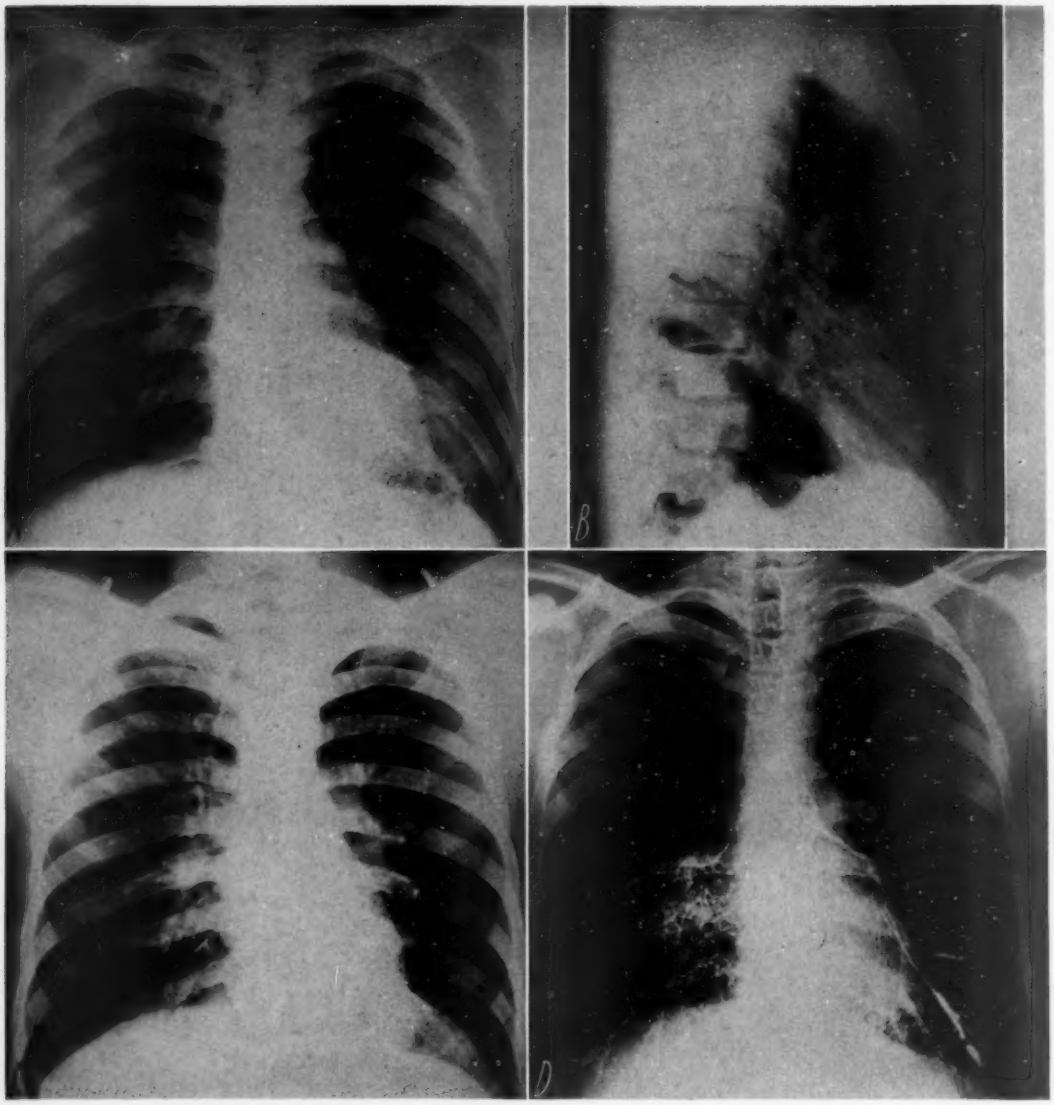


Fig. 7. *A*, portable anteroposterior roentgenogram shows a small patch of parenchymal infiltration at the left base medially and elevation of the left hemidiaphragm. *B*, same case eighteen days later shows resolution of the process and return to normal relationship between the domes of the diaphragm.



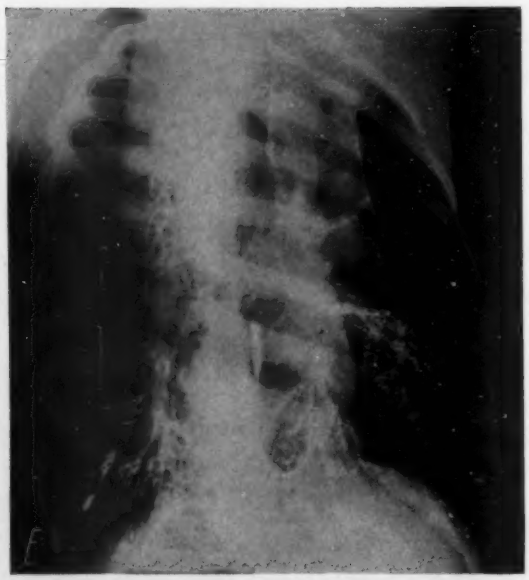


FIG. 8. *A* and *B*, portable anteroposterior and left lateral roentgenograms of chest show an area of homogeneous circumscribed pneumonia at the posterior and basal portions of the left lower lobe. *C*, same case sixty-two days later shows only partial resolution. *D* and *E*, posteroanterior and left oblique bronchograms thirty-nine days later show fusiform dilatation of a bronchus at posterior and basal segment of left lower lobe with failure of smaller bronchi to fill.

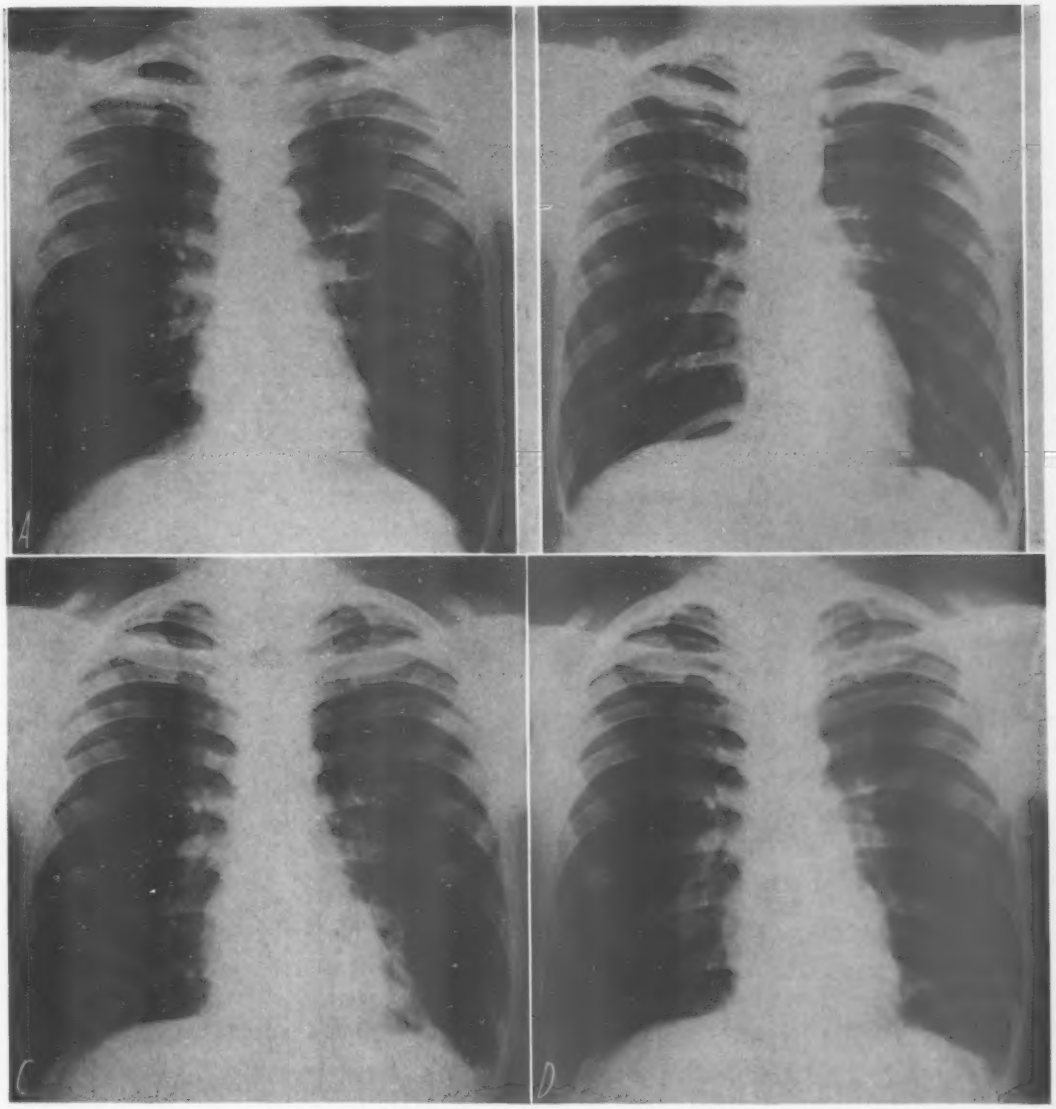


FIG. 9. *A*, evidence of parenchymal infiltration extending in a linear manner up and out from left hilum. *B*, same case twenty-seven days later in which there is demonstrated localized structural accentuation with hazy parenchymal infiltration at left base. *C*, same case ninety-nine days later. Pronounced and dense infiltration at left base; clinical evidence of asthma. *D*, twelve days later, partial resolution of pneumonic process.

Three of these showed clinical evidence of bronchiectasis. Lipiodol bronchograms were done in 2 cases and were confirmatory (Fig. 8). The 2 remaining cases showed roentgen evidence of non-resolution and clinical evidence of asthma (Fig. 9).

DISCUSSION

From the foregoing it is submitted that the condition described is identified with constitutional symptoms with localization in the respiratory tract which frequently advances to parenchymal infiltration. Clinical diagnosis at present should be termed "atypical pneumonia, etiology unknown."

Roentgen examination in positive cases reveals evidence of parenchymal infiltration, the extent of which does not coincide with the severity of the symptoms and is predominantly located in the lower lobes.

This series revealed localization in one lobe in the great majority.

The appearance of the infiltration is either transparent and homogeneous, flocculent or a combination of these, occasionally associated with hilum prominence. It is considered that this classification coincides with Scadding's "benign circumscribed" and "disseminated focal" types and this classification is endorsed.

When located in an upper lung field, the disseminated focal infiltrations resemble pulmonary tuberculosis of the confluent flocculent type and the benign circumscribed consolidation bears a close resemblance to the exudative, homogeneous tuberculous infiltration referred to in the German literature as the Assmann infiltration. A re-check roentgenogram in two weeks usually allows for a definite opinion lacking confirmatory clinical and laboratory data.

The use of the lateral projection has been of value. When one considers the volume of lung parenchyma located below the summit of the diaphragm and behind the heart which is not visible in the posteroanterior projection, the value of the appropriate lateral roentgenogram becomes increasingly apparent. Moreover, this projection provides an insight into the extent of the process and thereby serves to localize the infiltration accurately. Occasionally, consolidation is demonstrated only in this view. Finally, the lateral roentgenogram serves to differentiate the benign circumscribed infiltration from interlobar pleuritis.

Elevation of a hemidiaphragm in conjunction with a basal lesion has been encountered more frequently than in reports of others. While it is recognized that the finding may be due to a lack of elasticity incident to the coexistent inflammatory changes, a lobular or partial atelectasis seems more appropriate. The disease is characterized by a respiratory mucous membrane reaction with exudation in some stages. It is a reasonable conjecture that in a certain number plugging of bronchioles takes place with resulting atelectasis. Evidence of coexisting atelectasis gives rise to an appreciable prolongation in length of anatomical resolution. Further, in a few cases, the combination was followed by evidence of non-resolution and bronchiectasis. The importance of coexisting atelectasis is stressed, for if this becomes irreversible, the development of permanent bronchiectasis may follow.

Resolution, however, is the rule, leaving no sign of the previous infiltration and occurring on the average within two weeks. There are a few cases with roentgen evidence of non-resolution and clinical evidence of asthma. To date there has been no mortality.

Accordingly, the roentgenographic picture, while fairly characteristic, may show sufficient deviation to be confused with that of pneumococcus lobar pneumonia, bacterial bronchopneumonia, tuberculosis, pulmonary abscess, acute bronchiectasis, metastatic infiltration and, of course, the known virus and rickettsial diseases that involve the lung.

SUMMARY AND CONCLUSIONS

1. One hundred and seventy-eight cases of atypical pneumonia, with roentgen evidence of bronchopneumonia, are presented.

2. Scadding's roentgen classification of benign circumscribed and disseminated focal types is endorsed.

3. The occurrence of accompanying atelectasis is reported and its importance discussed.

4. The importance of the appropriate lateral projection of the chest is stressed.

5. Resolution is the rule. Accompanying atelectasis probably accounts for the rare development of bronchiectasis. Non-resolution with clinical evidence of asthma has also been observed.

REFERENCES

1. ACKERMANN, A. J. Roentgenological consideration of influenzal pneumonitis. AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *46*, 175–181.

2. Bowen, A. Acute influenza pneumonitis. Am. J. Roentgenol. & Rad. Therapy, 1935, *34*, 168–174.
3. Dingle, J. H., and Finland, M. Medical progress; virus pneumonias. II. Primary atypical pneumonias of unknown etiology. *New England J. Med.*, 1942, *227*, 378–385.
4. Kornblum, K., and Reimann, H. A. Roentgenological aspects of epidemic of acute respiratory tract infection. Am. J. Roentgenol. & Rad. Therapy, 1940, *44*, 333–344.
5. Levitin, J., and Brunn, H. Study of the roentgenologic appearance of lobes of the lung and interlobar fissures. *Radiology*, 1935, *25*, 651–680.
6. Ramsay, H., and Scadding, J. G. Benign broncho-pulmonary inflammations associated with transient radiographic shadows. *Quart. J. Med.*, 1939, *8*, 79–95.
7. Reimann, H. A. Acute infection of the respiratory tract with atypical pneumonia; disease entity probably caused by a filtrable virus. *J. Am. M. Ass.*, 1938, *111*, 2377–2384.
8. Scadding, J. G. Lung changes in influenza. *Quart. J. Med.*, 1937, *6*, 425–465.
9. Scadding, J. G. Disseminated focal pneumonia. *Brit. M. J.*, 1937, *2*, 956–959.
10. Seeds, A. E., and Mazer, M. L. Virus pneumonia; roentgenographic characterization of recent virus pneumonitis with bronchopneumonia. Am. J. Roentgenol. & Rad. Therapy, 1943, *49*, 30–38.

A PLEA FOR THE PREVENTION OF BRONCHIECTASIS*

By KARL KORNBLUM, M.D.
PHILADELPHIA, PENNSYLVANIA

THE JUSTIFICATION for this presentation is based upon the assumption that the general medical profession is not aware of the prevalence of bronchiectasis, nor does it appreciate the significance of this disease. That a roentgenologist should feel called upon to discuss the subject of the prevention of bronchiectasis is due to the belief that no specialist in the practice of medicine has a better opportunity to view this disease in all its varied aspects. To understand the need and the measures available for the prevention of bronchiectasis, one must have knowledge of the incidence, pathology, pathogenesis, etiology, symptomatology, clinical course, prognosis, economic importance and treatment of this malady. Bronchiectasis cannot be cured *in situ* and since surgical excision of the diseased tissue is limited to selected cases, it is obvious that the attack upon the problem of bronchiectasis lies in prevention rather than cure.

To a large part of the medical profession bronchiectasis is but a name and to a surprising number of physicians, it is a name they do not clearly understand. There is little wonder, then, that the prevalence and clinical significance of this disease is not generally appreciated. With a little thought, one can, I believe, recognize the reason for this state of affairs. If bronchiectasis were a new and startling disease, every practitioner throughout the land would be familiar with and interested in it. But bronchiectasis is an old disease and has, up to the present time, attracted the attention of only specialized medical groups. It has never been popularized as an affection of importance and general clinical interest. First described by Laennec in 1819, it was a disease which, for the next century, largely attracted the attention of pathologists who devoted much time to investigations of its pathology, pathogenesis and etiology. Since the condition was not readily recognized clinically, it attracted but little attention from practitioners, and treatment was a matter to which no thought whatever was given. With the introduction of the bronchoscope by Killian, of Vienna, in the 1880's and its perfection and popularization by Jackson and his disciples in this country during the early part of the present century, the study of the bronchial tree in the living subject became possible and opened up new vistas for clinical investigation. And with the aid of another remarkable and comparatively recent discovery, the roentgen ray, visualization of the bronchial tree by means of the insufflation of bismuth by Jackson in 1918 and later (1922) the introduction of iodized oil by Sicard and Forestier made possible the visualization of the anatomy of the bronchial tree in health and disease. These innovations may rightly be said to mark the real beginning of our understanding of the disease known as bronchiectasis.

There is yet another reason for the lack of recognition on the part of the general medical profession. The fact that the diagnosis of bronchiectasis remains largely in the hands of specialists does not tend to encourage interest on the part of the general practitioner. In the final analysis, a positive diagnosis can be made only by bronchography. This is a procedure that is not available to the average physician and one which is being carried out successfully in only the more modern and well equipped hospitals. With this state of affairs, the average physician thinks of bronchiectasis as a disease of interest only to the specialist such as the bronchoscopist, the radiologist, the internist specializing in chest diseases

* From the Department of Roentgenology of the Jefferson Medical College and Hospital, Philadelphia.

and the thoracic surgeon and thus comes to adopt the attitude that, to him, bronchiectasis is of no immediate concern. However, in this discussion we are not primarily concerned with bronchiectasis but rather with the conditions which may terminate in bronchiectasis. These are the diseases which constitute a large percentage of the work of the general practitioner. The recognition on the part of the general practitioner that many of the conditions which he sees daily are those which may develop into bronchiectasis should give him an immediate and first hand interest in this subject. And when he comes to realize that the prompt recognition and the proper treatment of the diseases which predispose to bronchiectasis are essential to its prevention, he will have come to the realization that while the specialist deals with the end results of this condition and can hope to cure only a small proportion, the key to the problem of prevention is in the hands of the general practitioner.

Why should radiologists concern themselves with the prevention of bronchiectasis and why are they in such an excellent position to view this disease in all its varied aspects? Roentgenography of the chest has become an indispensable procedure in the practice of medicine. Furthermore, its widespread use in survey studies of the chest in industry, in schools, and in the military services foreshadows the day when the yearly roentgen study of the chest of the entire population will be routine. Such surveys bring to light many conditions recognized today as forerunners of bronchiectasis and thus the roentgenologist has the opportunity to detect many individuals who may develop this disease. Bronchiectasis, although more prevalent in adults, is primarily a disease of childhood. The roentgenologist in his daily work with children can detect those conditions which often result in bronchiectasis long before any symptoms of this disease are present. The pediatrician who sees the patient during the developmental stage of bronchiectasis loses sight of the patient as an adult, now a victim of bronchiectasis. The internist may care for a patient during the illness destined to result in bronchiectasis but may not be called upon to see him when bronchiectasis has become established. The phthisiologist may have a patient referred to him for the diagnosis of tuberculosis, but in the absence of evidence of this disease he may or may not recognize the presence of bronchiectasis. The experience of the bronchologist is such that bronchiectasis is always uppermost in his mind. Unfortunately, by the time he is consulted the disease is usually well established and prevention is out of the question. The thoracic surgeon is in much the same position. The general practitioner will see the patient as a child or an adult and will encounter bronchiectasis in all of its stages. It is not, however, easy to connect the symptoms of the adult with full blown bronchiectasis with the relatively mild and inconsequential symptoms of the child with a mild tracheobronchitis following an attack of whooping cough or measles. The roentgenologist, on the other hand, sees the patients of all these specialists and of the general practitioner as well and in his daily work there are usually several patients who represent the various stages in the development of bronchiectasis. There is the child with the annoying cough and chronic nasal discharge; there is the internist's patient just recovering from pneumonia who has persistent definite roentgen changes at the site of the pulmonary involvement after clinical recovery is complete. The chest specialist has requested a roentgenogram of the young man who recently had a slight hemoptysis. Tuberculosis is suspected but the roentgenogram fails to substantiate this diagnosis. There is, however, definite intensification of the trunk shadows at both bases. The bronchoscopist refers a patient who has suffered from a chronic cough for many years. The chest roentgenogram reveals an unsuspected foreign body of the lung. The surgeon has requested a bronchography preliminary to a lobectomy for bronchiectasis. This series of cases, with its many varia-

tions, is a daily and familiar picture to the average roentgenologist. He is constantly confronted by the life cycle of bronchiectasis as a lesion of relatively little importance to the bronchographic picture of large bronchial dilatations and sacculations, and he cannot help but concern himself with its prevention.

To understand the need for the prevention of bronchiectasis one must have knowledge regarding its entire picture from the onset to its final termination and must know just what it means to an individual to have this affliction. A voluminous literature has come into being regarding every aspect of this malady. In digesting this material, one is impressed with the controversy surrounding almost every phase of the condition. There appears to be no unanimity of opinion regarding anything about bronchiectasis with the exception of its definition. All seem agreed that bronchiectasis is nothing more than a condition in which the bronchi show an abnormal dilatation. The extent or character of this dilatation, the amount of the bronchial tree involved, the duration of the condition, the presence or absence of symptoms and the possibility of complications have nothing to do with the definition. It would serve no useful purpose in this discussion to enter into all the controversial aspects of this disease, so an attempt will be made to adhere to more or less well established facts.

INCIDENCE OF BRONCHIECTASIS

Is bronchiectasis sufficiently prevalent and are its harmful effects such as to warrant the interest of every physician?

Bronchiectasis was formerly regarded as a comparatively rare disease. One gains some idea of this by consulting textbooks of pathology and medicine of some twenty to thirty years ago. A few paragraphs, rarely a page or so, was devoted to this condition. Contrast this with the space now devoted to a full discussion of every phase of bronchiectasis in modern textbooks, and the growing importance of this disease becomes readily apparent. This change has been brought about by our modern methods of diagnosis which reveal for the first time the real prevalence of bronchiectasis. And now with the remarkable advances being made in the surgical treatment of bronchiectasis, this disease is rapidly coming into its own.

It is surprising, however, how little is to be found in the literature regarding the incidence of bronchiectasis. Writers on the subject refer to the disease as being very common but apparently there are few statistics to prove this point. Leopold[19] states that the importance of bronchiectasis is attested by the fact that in frequency this disease stands second only to tuberculosis among chronic infections of the lungs. According to Hamman[15] postmortem statistics indicate that bronchiectasis is found in about 1.5 per cent of routine autopsies. Naturally, the diagnosis of bronchiectasis is more common in those clinics in which bronchoscopy is available. It must be remembered also that the published reports constitute, in the main, the more severe cases and that the vast majority of patients with bronchiectasis are dismissed by their physician with a diagnosis of chronic bronchitis, and then there is that even larger group of relatively mild cases who never seek medical attention. From these facts it can be seen that it is probably not possible to obtain a true estimate of the incidence of bronchiectasis.

However, certain facts regarding the incidence of bronchiectasis are fairly well established. While bronchiectasis shows no particular sex predilection, statistical studies indicate that the disease is slightly more common in males than in females. Farrell[10] reported cases in 52 males, 48 females; Perry and King,[20] 214 males, 186 females. This slight male predominance does not hold for children where the sexes are about equally represented. No age is immune to this disease. It has been found in the fetus and in the newborn at postmortem occurring as a congenital condition. It has been diagnosed clinically during infancy. Whether these cases represent congenital bronchiectasis with a superimposed infec-

tion occurring early in life, it is usually not possible to determine without histopathological study of the involved tissues. Approximately half the cases of bronchiectasis start before the age of ten but the disease is usually not recognized until years later. The incidence of bronchiectasis, therefore, increases with each succeeding decade until the third decade when it reaches its peak. Thus bronchiectasis is most common between the ages of twenty to thirty. During the next decade there is a gradual decline in frequency and after forty the disease becomes much less common but is to be found even in the aged. This age distribution distinctly emphasizes the fact that, although the majority of cases of bronchiectasis are diagnosed and treated during adult life, the onset of the condition occurs during childhood. Bronchiectasis is, therefore, primarily a disease of childhood.

PATHOLOGY OF BRONCHIECTASIS

Whenever the bronchial tubes are dilated beyond their normal caliber, there exists the pathological entity known as bronchiectasis. This condition does not ordinarily give rise to symptoms. Only when there is an associated infection do symptoms occur, and not until then can the clinical entity of bronchiectasis be said to exist. An exception to these facts is the occurrence of so-called dry bronchiectasis in which bronchial dilatation but no infection is present. This condition only manifests itself clinically in the occasional occurrence of pulmonary hemorrhages, so that the condition is also known as hemorrhagic bronchiectasis.

That inflammation of one or more bronchi initiates the process of acquired bronchiectasis is fairly well accepted by most authorities. This inflammation is almost invariably the result of infection. Upon the severity and extent of the infection will largely depend the subsequent course of events. If the resulting inflammation is severe enough to cause a desquamation of the epithelial lining of the bronchus with destruction of the underlying muscular and elastic tissues, then the groundwork for bronchiectasis has been laid. This ulcerative process may extend beyond the bronchus into the surrounding parenchyma of the lung. When healing is attempted by the regenerative powers of the lung, granulation tissue, rich in blood vessels, makes its appearance. These granulations are subsequently covered by a somewhat modified type of epithelium, without cilia. The bronchial wall is thus composed of this newly epithelized granulation tissue devoid of muscle and elastic fibers. The granulation tissue is subsequently replaced by fibrous tissue and this may extend for a variable distance into the lung parenchyma. The bronchial wall is thus considerably weakened and dilatation occurs resulting in bronchiectasis.

Bronchiectasis is a progressive disease since each pathological alteration predisposes to additional changes which intensify the condition; thus a vicious circle is created. The changes in the bronchial wall, the loss of the ciliated epithelium and the accompanying fibrosis prevent the elimination of bronchial secretions. The retained secretions become infected and intensify the changes already present. The disorderly and unrestrained production of granulation tissue, which subsequently may result in permanent folds, often causes partial or complete obstruction of the bronchial lumen, thus definitely interfering with respiratory function The ever present infection in bronchiectasis predisposes to the frequent occurrence of pneumonitis. This complication aggravates the existing bronchiectasis, tends to spread the infection to adjacent portions of the bronchial tree and upper respiratory tract and eventuates in a chronic interstitial or indurative pneumonia as well as a chronic tracheobronchitis.

As a result of the many factors involved, various types of deformity of the bronchi occur. These have been described as cylindrical, fusiform and saccular. The peribronchial and interstitial fibrosis resulting from bronchiectasis tends to distort and in-

crease the bronchial dilatation by direct traction upon the bronchial wall. At times the ulcerative bronchitis is so severe that the bronchial wall is perforated and cavities occur in the surrounding lung parenchyma. These cavities simulate the saccular dilatations of the bronchi. This condition is rightfully referred to as multiple lung abscess or chronic pulmonary suppuration which is often associated with or perhaps the cause or result of bronchiectasis. Finally gangrene of the lung may occur in association with bronchiectasis. The pathological changes as described are for the most part irreversible since the basic changes are primarily the destruction of tissues which show little tendency to regenerate.

The pathological changes of bronchiectasis vary considerably in extent and severity. These changes may be unilateral or bilateral, or they may involve only a small portion of a lobe. It is an interesting observation of Perry and King[20] that bronchiectasis shows little or no tendency to spread beyond the original site of involvement and that the pathological changes are usually maximal when first demonstrated. The fact that patients will become progressively worse clinically is due to the increase in the severity of the accompanying infection and the long continued toxemia which is so often present.

Most statistical reports of the anatomical distribution of bronchiectasis indicate that the left lower lobe is most frequently involved. This is particularly true in children. According to Leopold,[19] bronchiectasis in the left lung is three times as common as in the right in children and twice as common in adults. This predilection for the left lower lobe has been explained by Duken and von den Steinen[8] on the basis that the right lower lobe drains better than the left because the right main bronchus is a direct continuation of the trachea, that the left main bronchus is narrower than the right and shows a constriction where it is crossed by the left pulmonary artery and that in children this artery can readily compress the bronchus. These factors favor lobar collapse and retention of secretions in the left lower lobe.

PATHOGENESIS OF BRONCHIECTASIS

Infected, dilated bronchi constitute the basic pathological changes in bronchiectasis. The manner in which the bronchi become infected is readily understood. The weakening of the bronchial wall as the result of the pathological changes due to infection permits the bronchi to dilate. But what is the force which actually dilates the bronchi? This, without doubt, has been the most controversial aspect of bronchiectasis since the days of Laennec. Many theories have been advanced and although it is believed by some that the problem has been solved, there still continue differences of opinion. The changing views regarding the dilating force in bronchiectasis has been chronologically summarized by Hamman[15] as follows:

> This matter of the dilating force, which leads to bronchiectasis, when the bronchial wall is weakened by disease, has been commented upon and questioned by all authors who have written upon the disease. Medical literature is full of these discussions. Laennec, the first to describe the pathological anatomy of bronchiectasis, ascribed the condition to retained bronchial secretion. Andral, in 1827, emphasized the effects of inflammation upon the bronchial wall leading to attenuation and loss of elasticity. Apparently he thought the stress of ordinary breathing sufficient to dilate such weakened bronchi. Reynard, in 1838, apparently was the first to describe the association of bronchiectasis and bronchial obstruction. Corrigan, 1838, in his studies on cirrhosis of the lung, noted the frequent association of bronchiectasis with extensive fibrosis. He explained the bronchial dilatation as a result of the pull of the scar tissue. Rilliet and Barthez, 1843, were the first to call attention to the frequent occurrence of bronchiectasis in children and to emphasize the role of pneumonia, particularly pneumonia complicating measles and pertussis. Mendelsohn, 1845, contended that cough was the dilating force which produced bronchiectasis when the bronchial walls were weakened by disease. Barth, 1856, stressed again the importance of bronchial obstruction, contending that

all the factors previously invoked to explain the development of bronchiectasis were most effective in the presence of bronchial obstruction. Biermer, 1860, in his comprehensive review of bronchiectasis collected all the views previously maintained and stressed again the importance of bronchial obstruction. During the following sixty years, these opinions have been reviewed and revised with much discussion, and even today the discussion continues. However, during the past fifteen years accumulating evidence has favored the view that bronchiectasis is caused only by bronchial stenosis.

Thus, it is seen that before bronchiectasis can develop, not only is infection necessary but some form of bronchial obstruction must be present. Either bronchial infection or obstruction may be primary. When infection occurs first, bronchial occlusion may result from thick, inspissated secretions, granulation tissue or cicatricial changes in and about the bronchi. When bronchial obstruction is primary, the stagnation and retention of secretions invite infection.

By what mechanism does bronchial obstruction cause bronchial dilatation? When a bronchus becomes completely occluded, collapse of the pulmonary tissue peripheral to the obstruction occurs. The surrounding lung tissue becomes overaerated in order to occupy the space left by the collapsed tissue. Thus, there is created a disturbance in the pressure relationships within the chest, the effect of which is to exert traction upon the infected and weakened bronchi of the collapsed tissue sufficient to cause dilatation. When the lumen of a bronchus is only partially occluded there may be a ball-valve effect; that is, air readily enters the involved tissues during inspiration but is prevented from escaping by the bronchial occlusion during expiration. Thus, with each inspiration there is an ever increasing pressure within the involved lung tissue which may grow to considerable proportions. This is more than sufficient to dilate the weakened bronchi. With partial obstruction, in the absence of a ball-valve arrangement, bronchial dilatation will also occur. Since the inspiratory phase of respiration is more forceful than the expiratory phase, an increased pressure within the tissues supplied by the occluded bronchus, sufficient to dilate the bronchi, will occur. It is believed that in the presence of normal bronchi these forces are not sufficient to cause permanent dilatation. These effects of bronchial dilatation are more effective when the larger bronchi are involved since much more tissue becomes collapsed and the disturbance of intrathoracic pressure is greater. This fact is in conformity with the pathology of bronchiectasis since it usually is the larger and middle sized bronchi that are involved.

ETIOLOGY OF BRONCHIECTASIS

I. *Congenital*
II. *Acquired*
  A. *Bronchial Infection*
    1. *Acute tracheobronchitis*
    2. *Pneumonia*
      a. Bronchopneumonia
        (1) Influenza
        (2) Measles
        (3) Pertussis
      b. Lobar pneumonia
    3. *Chronic paranasal sinusitis*
    4. *Allergy*
  B. *Bronchial Obstruction*
    1. *Intrabronchial*
      a. Foreign body
      b. Broncholith
      c. Occluding secretions
    2. *Bronchial*
      a. Stenosis
        (1) Congenital
        (2) Acquired
          (a) Traumatic
          (b) Infectious
            Specific
            Nonspecific
      b. Tumor
    3. *Peribronchial*
      a. Enlarged lymph nodes
      b. Tumor
      c. Pulmonary fibrosis
  C. *Miscellaneous*
    1. *Lesions of the pleura*
    2. *Lesions of the thoracic cage*

Congenital Bronchiectasis. Although there has been considerable controversy regarding the existence of congenital bronchiectasis, the finding of dilated bronchi in the lungs of the fetus and in newborn infants at autopsy leaves little doubt that this condi-

tion does occur. In the absence of infection it is highly improbable that these cases would give rise to symptoms. When infection is present it is difficult to determine whether the bronchial dilatation is congenital or acquired. The mere fact that clinically demonstrable bronchiectasis may occur a few weeks after birth does not justify the assumption that the condition is congenital since it has been amply shown that under proper conditions bronchiectasis may develop quite rapidly. The etiological factors underlying the production of congenital bronchiectasis are but little understood.

Acquired Bronchiectasis. In acquired bronchiectasis it is generally conceded that bronchial infection and bronchial obstruction are the most important etiological factors. There is the growing belief that a combination of the two is present in every case and that one without the other would probably not result in bronchiectasis. This would account for the fact that the majority of cases of either infection or obstruction do not give rise to bronchiectasis. Either infection or obstruction may be the primary lesion, the other resulting as a complication.

This etiological origin directs attention to the fact that bronchiectasis is never a primary disease but is always secondary to some pre-existing condition. The primary disease may dominate the clinical picture, bronchiectasis occurring as an unimportant complication such as is the case in pulmonary tuberculosis or in most cases of lung abscess. In other instances, however, the primary condition may quickly subside; bronchiectasis appears years later and is then regarded as an independent disease. Such is often the case in bronchiectasis which follows pneumonia.

A. *Bronchial Infection.* From the standpoint of infection an acute tracheobronchitis, either alone or as an accompaniment of a pneumonia, is the basis for the initiation of the changes leading to bronchiectasis. In the history of bronchiectatic patients the onset from a specific illness is to be found in more than half the cases. Warner[24] reported 59 per cent, Diamond and Van Loon[7] 63 per cent. The condition which appears most prominent in such histories is pneumonia (Raia[21] 67 per cent, Warner[24] 30 per cent). Of the different types of pneumonia, bronchopneumonia is the most common offender. In a severe attack there may be an accompanying ulcerative bronchitis. In less severe cases of acute tracheobronchitis and bronchopneumonia, the patient may be left with a chronic tracheobronchitis and develops a predisposition to repeated attacks of respiratory tract infection which eventuate in a bronchiectasis.

Acute tracheobronchitis and bronchopneumonia are frequent complications of such common infections as influenza, measles and whooping cough. As such they may lead directly into bronchiectasis or may leave the patient with a chronic tracheobronchitis. Influenza, in particular, is regarded by some investigators as especially prone to result in bronchiectasis. It is to be remembered that in these acute respiratory tract infections it is not the infection alone which causes the bronchiectasis but the patchy areas of atelectasis due to occluding secretions that supply the mechanism for the dilatation of the bronchi in the involved areas.

Whereas the preceding conditions are common etiological factors to be found in children, lobar pneumonia is occasionally responsible for the bronchiectasis having its onset in adult life. It is common knowledge that atelectasis of varying degree is an essential part of the pathological changes occurring in a lobar consolidation. Many authors, with varying degrees of emphasis, have directed attention to the importance of atelectasis in the production of bronchiectasis. The large bronchi involved in an area of atelectasis do not become collapsed. They thus become subjected to the stress and strain of the respiratory movements of the chest and, weakened by infection, dilatation readily occurs. This is particularly prone to occur in slowly resolving pneumonias.

Lobar pneumonia less commonly results in a chronic tracheobronchitis but in this regard it may also initiate the vicious circle of respiratory tract infections leading to bronchiectasis. Failure of complete resolution in lobar pneumonia is of common occurrence. The local bronchitic and parenchymal changes that constitute the pathological picture of an unresolved pneumonia are such as would readily terminate in a bronchiectasis.

When one thinks of a lung abscess, instinctively the possibility of a tonsillectomy as the etiological factor is considered. This association is a well established medical fact. That bronchiectasis may occur as a complication of tonsillectomy is less generally known. It is, however, an etiological factor which must be given some consideration. In the 400 cases of Perry and King,[20] 43, or 11 per cent, followed tonsillectomy and adenectomy. This type of bronchiectasis probably also originates as an acute respiratory tract infection, either in the form of a bronchopneumonia or lobar pneumonia.

Chronic Paranasal Sinusitis. Considerable attention has been given to the relationship of disease of the paranasal sinuses and pathological conditions of the lung. That such a relationship exists there can be no doubt but as regards bronchiectasis some of the more recent writers have taken issue with those authorities who maintain that sinusitis is one, if not the most important, predisposing cause of bronchiectasis. Goodale[12] and also Clerf[6] have emphasized the importance of sinusitis in the etiology of bronchiectasis. Erb,[9] on the other hand, is of the opinion that sinusitis follows rather than precedes bronchiectasis in most instances. Nevertheless it cannot be denied that sinusitis is an important factor in the development of bronchiectasis. The frequency of the "common head cold" with involvement of the paranasal sinuses, the tendency of the sinuses to harbor infection and to become chronically involved and the tendency of the chronically infected sinuses to act as a source of reinfection for the rest of the respiratory tract leading to a chronic tracheobronchitis has been well established. This predisposes to attacks of pneumonia from which bronchiectasis may develop. The fact that many individuals with chronic sinusitis never develop clinical evidence of bronchiectasis is no argument against the relation of the two conditions.

The frequent association of sinusitis and bronchiectasis has been an outstanding feature of many statistical studies. Thus, Farrell[10] found 86 per cent of his series of bronchiectatic patients with sinus involvement; Diamond and Van Loon[7] report 64 per cent, and Raia[21] 82 per cent. It must be remembered, however, that the mere association of sinusitis with bronchiectasis is no justification for the conclusion that the sinusitis caused the bronchiectasis. There may be no connection whatever. On the other hand, there is no denying the fact that paranasal sinusitis often results from a bronchiectasis. The continual drainage of infected material from the dilated bronchi aggravates the existing bronchitis which spreads by continuity until the entire respiratory tract becomes involved including the nasal accessory sinuses. This sequence of events seems inevitable. The coexistence of sinusitis and bronchiectasis leads to a vicious circle, an exacerbation of the infection in one area resulting in an acute flare-up in the other. This has been convincingly demonstrated by Graham[13] in the study of patients with bronchopleural fistulae wherein it was found that an acute sinusitis resulted in aggravation of the inflammatory process and increase in the secretions from the bronchopleural fistula.

Allergy. One rather hesitates to discuss the relationship of bronchiectasis and allergy of the respiratory tract as manifested in asthma and hay fever. There are those who deny any relationship, while others regard allergy as an important etiological factor in the development of bronchiectasis. Watson and Kibler[25] studied a series of 46 cases of bronchiectasis and found that a large percentage had evidence of allergy. They noted that in the majority of pa-

tients, bronchiectasis was favorably influenced by treatment of the allergy. They directed attention to the close roentgenological resemblance of bronchiectasis and basal allergic bronchitis which can only be differentiated by bronchographic studies. They also stated that the common association of sinusitis and bronchiectasis can be explained on the basis of allergy.

When one considers the effects of hay fever and asthma upon the respiratory tract it would seem logical to expect bronchiectasis to follow as a complication of these conditions. The vasomotor phenomena which occur in the nose and paranasal sinuses as the result of allergy predispose these structures to infection. The common association of chronic sinusitis and hay fever bears witness to this fact. Similar factors operate in the lungs in patients with asthma. In well established cases, a chronic tracheobronchitis is an almost invariable accompaniment. This is readily demonstrated upon roentgen examination of the chest in individuals with asthma. The appearance of a severe chronic tracheobronchitis as manifested by an intensification of the hilar and truncal shadows of the lungs is often sufficiently characteristic to suggest that the patient is asthmatic. That the chronic tracheobronchitis, associated with atelectasis which so commonly occurs in asthma, should not result in bronchiectasis does not seem reasonable since all the factors necessary for its production are present.

B. *Bronchial Obstruction.* There is ample evidence both clinically and pathologically that bronchial obstruction is a prime factor in the etiology of bronchiectasis. The causes of bronchial obstruction are legion and are best considered from the standpoint of their relationship to the bronchus. The mechanism of the production of bronchiectasis by bronchial obstruction has already been considered. We need here merely to give attention to the specific forms of bronchial occlusion.

1. *Intrabronchial Obstruction.* In this category foreign bodies stand out as being particularly significant. All manner of foreign bodies gain access to the lungs and come to rest in one of the larger bronchi where a variable degree of obstruction is produced. With complete obstruction atelectasis occurs distal to the obstruction. With partial occlusion there is retention of secretions producing the so-called "drowned lung" and with a ball-valve type of obstruction there occurs an obstructive emphysema. Atelectasis, retained secretions and emphysema are recognized factors in the etiology of bronchiectasis. Whether or not a foreign body will produce a bronchiectasis is dependent upon several associated factors. Infection accompanying or resulting from the lodgment of a foreign body is necessary and the duration of the sojourn of the foreign body in the bronchus is also of prime importance. The longer the bronchial obstruction, the more severe and extensive the resulting changes and the more likely the development of bronchiectasis. Obviously bronchiectasis is more common in those instances in which there is no definite history of the aspiration of a foreign body, which may have occurred months or years before. This type of case is surprisingly common as revealed by roentgenologic and bronchoscopic studies.

Various writers have directed attention to the significance of broncholiths in the etiology of bronchiectasis. The frequency of this occurrence would be difficult to determine. The mechanism involved is similar to that operative in the case of extraneous foreign bodies.

Bronchial occlusion by mucous plugs and inspissated secretions is of fairly common occurrence and therefore important in the etiology of bronchiectasis. This is the cause of atelectasis in pneumonia and in postoperative patients. Such an occurrence is not uncommon in bronchial asthma nor in bronchiectasis itself. This type of bronchial obstruction may be encountered in almost any type of pulmonary infection.

2. *Bronchial Obstruction.* Lesions which involve the bronchial wall directly are not uncommon. Stenosis of a bronchus may

arise from a variety of causes. It may be congenital and as such may be one of the causes of congenital bronchiectasis. In the acquired variety stricture may be of traumatic origin, such as occurs from the lodgment of a foreign body, particularly those having sharp points. During the removal of a foreign body trauma of sufficient severity may occur to a bronchus to result in a stricture.

Stenosis may also arise during an acute respiratory tract infection from a fairly localized ulcerative bronchitis. With subsequent healing and scar tissue contraction strictures of varying degree may result. The infection may be of specific origin, such as tuberculosis or syphilis. Tuberculous granulations within the bronchi may produce multiple strictures. Syphilis is sometimes referred to in the etiology of bronchiectasis. This is not due to the specific infection itself but to a bronchial stenosis which is prone to occur in this condition.

Tumors of the bronchial wall are being encountered with increasing frequency. They may be either benign, in the form of an adenoma or papilloma or malignant, as a bronchogenic carcinoma. The latter are much more common. These tumefactions readily occlude the lumen of the bronchus, produce atelectasis, invite infection and thus initiate the changes essential for the development of bronchiectasis.

3. *Peribronchial Obstruction.* Peribronchial obstruction occurs as the result of extrinsic pressure upon a bronchus. Anything capable of producing this type of pressure may cause bronchiectasis. While there are many possibilities in this regard only a few of the more common need be mentioned here.

Enlarged lymph nodes occurring in the hilar region, from whatever cause, may produce sufficient pressure upon one or more of the larger bronchi to cause partial occlusion. This interference with pulmonary ventilation favors the retention of bronchial secretions, invites infection and may ultimately lead to bronchiectasis. This sequence of events has been growing in importance with many recent writers on the subject. It affords an adequate explanation for the predominance of the onset of bronchiectasis in children. Enlargement of hilar lymph nodes is of common occurrence in children from such conditions as pertussis and tuberculosis.

Tumors in the mediastinum, hilum or parenchyma of the lung will, by direct pressure or invasion, occlude one or more bronchi and as in the case of enlarged lymph nodes the stage is set for the development of a bronchiectasis. Such tumors may be of various kinds, benign or malignant, and include aneurysms of the aorta and the tumefactions of lymphoblastomata.

Pulmonary fibrosis, which is such a common pathological entity, is capable of causing peribronchial obstruction. Corrigan, 1838, regarded cirrhosis of the lung due to pulmonary fibrosis as the cause of bronchiectasis. This theory is not now generally accepted although there remain some adherents to this idea. It has been pointed out that pulmonary fibrosis usually follows rather than precedes bronchiectasis. It is generally agreed, however, that pulmonary fibrosis is a contributory factor in bronchiectasis operating in two ways: by producing peribronchial occlusion and direct traction on the bronchial wall. Outstanding in this respect is the fibrosis so commonly associated with tuberculosis in which bronchiectasis to some degree is an invariable accompaniment. While certain authors have emphasized the pulmonary fibrosis of pneumoconiosis, it is certain that bronchiectasis does not often assume clinical significance in this condition. Possibly the element of infection is not sufficient to produce symptoms of bronchiectasis.

C. *Miscellaneous.* Of minor if not of questionable significance are certain miscellaneous conditions to which bronchiectasis is sometimes attributed. Lesions of the pleura, particularly adhesions, are sometimes mentioned as playing an important rôle. Such adhesions are supposed to exert sufficient traction upon the bronchi during

respiratory movements to cause dilatation. It is doubtful whether such a mechanism alone could produce bronchiectasis. Much more probable is the supposition that the pulmonary condition responsible for the pleural adhesions is the causative factor of a resulting bronchiectasis. Significant is the observation that bronchial dilatation does not occur in long continued pneumothorax and apparently bronchiectasis does not occur in long standing pleural effusions in which the lung is continuously compressed.

In much the same category is the relation of congenital and acquired deformities of the thoracic cage to bronchiectasis. Supposedly there is a weakening of the respiratory effort in the presence of thoracic deformities which leads to bronchial dilatation. The bronchiectasis which is sometimes seen associated with such conditions is most probably not due to the thoracic deformity *per se*. Deformities of the chest are at times of such a nature as to interfere with the normal physiology of respiration. This will, of course, predispose to respiratory tract infections and such infections are more probably the cause of any resulting bronchiectasis. Under such conditions, however, the thoracic deformity must be regarded as a contributory factor.

BACTERIOLOGY OF BRONCHIECTASIS

The etiology of bronchiectasis has been repeatedly sought for in the bacteriology of this disease. Claims have been made from time to time that certain organisms are directly responsible for the occurrence of bronchial dilatation. Thus Smith[23] has emphasized the importance of fusospirochetal infection. It is true that the Vincent's organism has a greater destructive effect upon the bronchial wall than most other organisms, but most observers are of the opinion that these organisms are secondary invaders, especially in view of the fact that they are more commonly found in the bronchiectasis of adults than of children. The frequency of Vincent's infection in the mouth of adults is common knowledge. In bronchiectasis a large variety of bacteria are to be found which vary from time to time and seldom is one organism present in pure culture. Most observers agree with Greey[14] that there is nothing specific in the bacteriology of bronchiectasis.

SYMPTOMATOLOGY OF BRONCHIECTASIS

The cardinal clinical manifestations of bronchiectasis are a chronic productive cough, the expectoration of variable amounts of sputum which may or may not be fetid, and occasional hemoptysis. Many inconstant and variable signs and symptoms may be present, such as recurring bouts of fever, dyspnea, night sweats, anemia, loss of strength and weight. The symptomatology is largely dependent upon the extent of the disease and severity of the infection. In the milder forms there may be no symptoms whatever. This is particularly true of so-called dry bronchiectasis in which there is dilatation without infection.

In the typical case of bronchiectasis, because of the constant infection present there is an excess amount of bronchial secretion. In an attempt to eliminate this material a chronic cough develops. This is almost invariably much worse upon arising in the morning due to the accumulation of secretions during the night. Patients often learn that by assuming certain postures drainage of the accumulated secretions can be facilitated. After such drainage the patient may be fairly free of cough for the remainder of the day. The amount of the sputum is a variable one depending upon the severity of the infection. At times it is very copious, thick, tenacious and difficult to raise.

The retained secretions serve as an excellent medium for a host of bacteria, many of them saprophytic in nature. According to Jackson and Jackson,[16] these serve to decrease the viscosity of the sputum so that it can be more readily expelled. This putrefactive process causes the sputum to be very foul and offensive. The odor is said to be due to the presence of a fusospirochetal infection. Considerable emphasis has been

placed upon this feature of the condition since upon this one factor alone the diagnosis of bronchiectasis can be suspected although offensive sputum also occurs in pulmonary abscess, chronic pulmonary suppuration and gangrene of the lung but usually in a more exaggerated form. Although a copious and fetid sputum is characteristic and almost invariably present in the advanced stages of the disease it should be remembered that such sputum is not present in the majority of cases of bronchiectasis. Warner[24] found that in only 20 per cent of his cases was there a daily production of 4 ounces or more of foul smelling sputum. One characteristic which he regards as more important and extremely suggestive of bronchiectasis is the "chunky" nature of the sputum. Nevertheless, the importance of the foul and fetid sputum of bronchiectasis cannot be minimized since it is the one feature of the disease which makes the condition such a loathsome one for both the patient and those with whom he comes in contact. Jackson and Jackson[16] have likened the condition to a septic tank.

It is not sufficiently appreciated that bronchiectasis is one of the most common causes of hemoptysis. This is particularly true in children. Blood spitting occurred in 45 per cent of the cases reported by Warner.[24] To the average physician, bleeding from the lung means tuberculosis. No one has a better opportunity to appreciate this fact than the roentgenologist. A request for a chest roentgenogram in a patient with blood spitting is usually accompanied by a diagnosis of tuberculosis. The two conditions, aside from tuberculosis, which must be looked for in the roentgenogram in such cases are bronchiectasis and mitral stenosis. It is surprising the number of such cases encountered by the roentgenologist in which the diagnosis of tuberculosis has been made by the clinician.

If one recalls the pathology of bronchiectasis the basis for hemoptysis is readily understood. The fresh, highly vascularized granulation tissue which is so abundantly present in bronchiectasis shows a tendency to bleed quite readily. The irritating, harassing cough produces sufficient trauma to these granulations to cause them to bleed occasionally. The bleeding is usually not very great in amount. A mere streaking of the sputum with blood may be all that is present but it may recur quite frequently. At times, however, quite a profuse hemorrhage may occur and this may prove to be a serious complication.

Depending upon the amount of bronchial secretions and the difficulty with which it is eliminated, there may be a low grade fever and the patient may become septic. With the establishment of adequate drainage these symptoms disappear. The constant absorption of septic material produces a state of low grade toxemia. This eventually leads to anorexia, a poor state of nutrition, a progressive anemia, and loss of weight and strength. Since bronchiectasis is a progressive disease there is an inevitable impairment of respiratory function leading to a variable degree of dyspnea. The inevitable myocardial damage resulting from the increased resistance within the lesser circulation incident to the pulmonary fibrosis of bronchiectasis plus the prolonged state of toxemia adds materially to the patient's signs and symptoms.

PHYSICAL EXAMINATION IN BRONCHIECTASIS

In comparison with the extent and severity of the pathological changes the physical signs in bronchiectasis are rather negligible. There are no signs which are pathognomonic. In the more advanced cases some restriction in the movement of the chest may be noted, there may be some dullness to percussion over the involved portions of the lung and the breath sounds may be somewhat less audible. Râles occasionally may be heard but are by no means constant. In long standing cases clubbing of the fingers characteristic of chronic pulmonary suppuration appears and the changes of chronic pulmonary osteoarthrop-

athy may be present. Eventually amyloidosis may develop.

DIAGNOSIS OF BRONCHIECTASIS

Only in the advanced cases are the symptoms sufficiently characteristic to warrant a diagnosis of bronchiectasis. In the mild and moderately advanced cases, which constitute the vast majority of patients, the symptoms may be merely suggestive. Of greater significance is the history of a definite onset during childhood from some specific infection, leaving the patient with a predisposition to frequent respiratory tract infections, a chronic cough which gradually becomes worse, accompanied by an increasing amount of expectoration. With such a history the diagnosis of bronchiectasis is most probable and a roentgen examination of the chest is in order.

The ordinary roentgenogram of the chest will not, as a rule, warrant a positive diagnosis of bronchiectasis. When this disease can be recognized in the ordinary roentgen study, the condition has reached an advanced stage. When viewing roentgenograms in a suspected case of bronchiectasis the possibility of a foreign body should never be forgotten. Quite characteristic of bronchiectasis are the dense triangular shadows frequently found in the base of a lung adjacent to the heart. Usually an intensification of the hilar and trunk shadows especially those to the bases is all that is found in the plain roentgenogram. This is indistinguishable from a chronic tracheobronchitis. Such findings in a child or young adult combined with a history as aforementioned warrants a suggestive diagnosis of bronchiectasis. The next step in the investigation is a bronchoscopic examination.

A bronchoscopic examination is an absolute essential in every patient with suspected bronchiectasis. This will reveal information not obtainable in any other way. One sees the condition of the respiratory tract from the larynx to the larger bronchi and learns whether these parts are involved by the inflammatory process and the extent and severity of this involvement. The presence of congenital anomalies can be detected, and important in every case of bronchiectasis is the presence of a foreign body. The actual site of the bronchiectasis is not reached by the bronchoscope so that the bronchial dilatations are rarely seen. The character of the inflammatory reaction and the aspiration of considerable amounts of thick, viscid, purulent secretions from the smaller bronchi are highly suggestive of bronchiectasis. Thus, while a definite diagnosis of bronchiectasis cannot be made by bronchoscopic examination, except in the advanced cases, the findings are usually such as to indicate the need for bronchography

The roentgen visualization of the bronchial tree after the introduction of a contrast medium is becoming of increasing value in all manner of pulmonary conditions. In bronchiectasis it is the only absolute method of establishing the diagnosis regardless of the stage of the disease. A number of methods have been devised for introducing the iodized oil into the bronchial tree. All give good results depending upon the skill of the physician performing the procedure. By means of bronchography the extent and nature of the bronchial dilatation are readily ascertained. It can be learned whether the disease is sharply localized, whether it involves more than one lobe and whether it is unilateral or bilateral.

In the final analysis, therefore, while there are many factors which may lead the clinician to suspect bronchiectasis, the diagnosis must actually be established by bronchography.

CLINICAL COURSE AND PROGNOSIS OF BRONCHIECTASIS

Bronchiectasis is primarily a disease of childhood, runs a slow progressive course, becomes clinically established during adolescence or early adult life, leads to a life of chronic invalidism and terminates in death from one of a number of complications. The condition has its onset during

childhood resulting from a combination of respiratory infection and bronchial occlusion. The disease may run a very rapid course becoming well established and easily recognized within a few weeks or months. The usual course of events, however, is much more insidious, the patient enjoying comparatively good health for many years after the onset of the condition but showing a greater predisposition to respiratory tract infections than the average individual. These infections increase in frequency and severity until adult life is reached when a well established bronchiectasis has resulted. In about two-fifths of such cases the initial condition responsible for the bronchiectasis has long since been forgotten.

The subsequent history regardless of whether the development has been rapid or slow is fairly characteristic. The patient's general health may be good but there is a tendency to "take cold" rather easily. These "colds" become increasingly difficult to "throw off." The patient is left with a persistent, annoying cough in between attacks of respiratory tract infection. The cough becomes somewhat productive. The sputum increases in amount and eventually becomes fetid and foul in character. The patient has increasing difficulty in raising the sputum and soon learns that this can be facilitated by assuming certain positions. His symptoms are worse in the morning. He never feels quite up to par and at times he is distinctly toxic. His general health begins to fail, he suffers from lassitude and ready fatigability, there is a loss of appetite and gradual loss of weight and strength. The development of this state of affairs may occur rapidly in the course of a few years or, on the other hand, the progression may be very slow covering a period of twenty to twenty-five years.

Eventually other systems of the body become involved, especially the cardiovascular system, the symptoms of which are superimposed upon those of the bronchiectasis. The terminal event is usually in the form of some complication which is fairly common. The patient becomes subject to repeated attacks of pneumonia. In Warner's[24] series 52 per cent had at least one attack of pneumonia and 27 per cent had more than one attack. One such attack may be severe enough to end fatally. Cardiac failure is a frequent cause of death in long standing cases. Massive pulmonary hemorrhage is the cause of a fatal termination in some cases. Brain abscess is a notorious complication in suppurative conditions of the lung and usually proves fatal. General debility and asthenia with a terminal hypostatic pneumonia may be responsible for the bronchiectatic demise.

Bronchiectasis is, however, not necessarily fatal. Although it is a progressive and irreversible disease it may at times become arrested or its progress may be so slow that the patient may live his allotted span of life and die from some other cause. In general, however, the prognosis of untreated bronchiectasis is poor.

The prognosis of bronchiectasis varies considerably in individual cases. Warner, in a series of 110 cases, reported a mortality of 23 per cent, with the average duration of the disease of nine years. Roles and Todd[22] report a general mortality, regardless of treatment, of 38 per cent. The mortality rate as reported by Perry and King[20] was 31 per cent. In the series of 171 cases reported by Bradshaw, Putney and Clerf,[5] 34.5 per cent died from bronchiectasis or its complications, with the average duration of the disease thirteen and a half years.

ECONOMIC IMPORTANCE OF BRONCHIECTASIS

As has been stated, the patient with a definitely established bronchiectasis becomes a chronic invalid. The frequently recurring attacks of respiratory tract infection cause much loss of time from work. This may make it difficult for an individual to hold a worth while position. The harassing cough and particularly the offensive sputum makes the individual objectionable to those with whom he is required to work. The toxicity and general lassitude so commonly present definitely interfere with the

individual's efficiency. He becomes painfully aware of his condition, of his inability to maintain his place in the world and to meet his social and economic obligations. This state of affairs has in some instances been terminated by suicide. It is important that physicians should recognize these facts. Thus the need for the prevention of bronchiectasis becomes all the more apparent.

TREATMENT OF BRONCHIECTASIS

Until recent years, the treatment of bronchiectasis was entirely medical. The most important single item in this form of therapy is postural drainage to rid the lungs of their septic material and to prevent toxemia. Many patients can be kept fairly comfortable by this one method alone. Sedation to control the annoying cough and to insure the patient rest and sleep is an important factor in treatment. Expectorants may aid in expelling the thick, tenacious sputum. In the presence of fusospirochetal infection the intravenous injections of neoarsphenamine have been found useful, especially in overcoming the fetor of the breath. Creosote by mouth has been used for the same purpose. General supportive measures to maintain health is of vital importance and must be combined with whatever therapy is employed. Precautionary measures to prevent or minimize the severity of the recurrent respiratory tract infections are of the utmost importance. As will be recognized, medical treatment is but palliative and not curative. No specific therapy in the form of sera or vaccines has been found of any avail. There has not yet been sufficient experience with the use of sulfonilamide and its derivatives to know whether or not these drugs will be of benefit in the treatment of bronchiectasis.

With the advent of the bronchoscope a new form of therapy for bronchiectasis was introduced, namely bronchoscopic drainage. This has been of inestimable value. It accomplishes in a much more efficient manner what the physcian has attempted to do with postural drainage. There is no question that the patient relieved of the germ laden secretions will be very much improved, subjectively and objectively, the progress of the disease will be much delayed and some of the complications may be prevented. The direct injection of drugs into the bronchial tree has not as yet proved of definite value, although there is the impression that patients are sometimes improved after the use of lipiodol for bronchography. Bronchoscopic drainage does not materially alter the underlying pathological changes of bronchiectasis; therefore, the condition is not cured by this form of therapy.

In 1934 Berck[1] reported his experience with radiation therapy in the treatment of bronchiectasis. This was followed by a second paper in 1937 by Berck and Harris[2] in which they reported definite improvement in a large percentage of the patients treated. According to these authors, the rationale for the use of this method is an attempt to change an infected and overproductive type of bronchiectasis into the dry form of the disease. It is well known that if the secretions can be minimized there is a marked improvement in the patient's symptoms and general physical condition. This method of therapy has not become very popular and there are few reports to substantiate the claims of the originators of the method.

The most recent addition to the therapy of bronchiectasis is surgery in which the involved lobes of the lung are removed. Other forms of surgery such as pneumothorax, phrenicectomy and thorocoplasty have also been tried but none of these have been of permanent benefit except in isolated cases.

The success of lobectomy and pneumonectomy is dependent upon a number of factors, such as the proper selection of cases, the general condition of the patient and the skill of the surgeon. The most favorable cases are those in which the disease is unilateral and limited to one lobe. The least favorable are those in which the disease shows a widespread bilateral involvement.

In these, even though the lobes most involved are removed, the entire respiratory tract is more or less involved by the underlying inflammatory process responsible for the bronchiectasis. In such cases, although considerable palliation can be accomplished by surgery, actual cure of the condition is impossible.

The general condition of the patient is of the utmost importance in the surgical treatment of bronchiectasis. Obviously a patient who is much debilitated, emaciated and anemic is a poor surgical risk and will not have the stamina nor the recuperative powers to withstand a formidable operation. Therefore, it is important that operation be not too long delayed and should be done before the patient begins to show systemic effects of the disease. In some advanced cases it may be necessary to restore the patient to an improved physical state before operation is attempted. Certain it is that surgical results will be much better the earlier operation is performed; this means a resort to surgery during childhood in many if not most of the cases. It is difficult to convince the referring physician to submit his patient to a major thoracic operation for a disease which in its earlier stages does not appear to be so very serious. Much education of the general medical profession regarding bronchiectasis is needed before the general practitioner will understand and have the proper attitude toward the surgical treatment of this disease.

The question arises as to whether surgery should not be done as soon as the diagnosis of bronchiectasis has been established. In view of the variable course of the disease in different individuals it would appear more logical to keep the patient under observation for a time and attempt to control the progress of the condition by less radical means. While definite progression is the rule in clinical bronchiectasis, at times this progression is so slow that the condition never becomes of serious import. Conservative measures should not be persisted in if the patient does not show definite improvement or the disease does not become arrested within a reasonable period of time.

Finally, one must consider the fact that a lobectomy or pneumonectomy carries with it a certain mortality. According to Bradshaw, Putney and Clerf,[5] the general mortality is about 10 per cent. In unilateral involvement the mortality is under 5 per cent. This is a matter which must be seriously considered when operation is advised. Furthermore, complications, such as empyema and bronchopleural fistula, may occur. Thus the skill of the surgeon plays a vital part in the success of the surgical treatment of bronchiectasis. The thorax is one of the most recent parts of the body to be invaded by the surgeon. Not all surgeons are trained in chest technique; therefore mortality statistics will vary widely. It must be remembered that only the expertly trained thoracic surgeon publishes his mortality statistics. Thus, the choice of a surgeon becomes vitally important when operation for bronchiectasis is being considered.

Surgery has outmoded the statement of Boyd,[3] "Once bronchiectasis is well established in childhood an early death from bronchopneumonia can only be regarded as a blessing." While surgery has very definitely improved the prognosis of bronchiectasis, surgery does not solve the problem of this disease since it is admitted by all that there are many cases not suitable for surgery. No precise statement has been found indicating the percentage of patients with bronchiectasis suitable for surgical treatment. Inquiry of several thoracic surgeons reveals a wide difference of opinion, ranging from 25 to 75 per cent. Bradshaw,[4] from his large experience in the surgical treatment of bronchiectasis, believes that not more than 25 per cent of patients are suitable for surgery when the disease is first diagnosed. He is impressed with the advanced stage of the disease when the patient first seeks medical attention, even when the history of the condition is of relatively short duration.

If one were arbitrarily to assume that

only unilateral cases of bronchiectasis are suitable for surgery, which is of course not true, some idea as to the percentage of patients in whom surgical treatment could be used might be obtained by reference to the anatomical distribution of the disease as reported by various authors. Thus, of the 979 cases collected from the literature by Leopold,[19] in 686 the disease was unilateral. Therefore, approximately 70 per cent would be suitable for surgery. There is considerable range among the authors quoted; thus, in the 60 cases of Block and Francis, 53 per cent were unilateral while in the 167 cases reported by Duken and von den Steinen, 81 per cent were unilateral. This latter series included children only. From this method of deduction it would appear that for about 30 per cent of patients with bronchiectasis there is at present no hope of cure. This further emphasizes the necessity of prevention.

This discussion of treatment has been based upon the generally accepted concept that bronchiectasis is a progressive and irreversible disease. No consideration has been given to the condition referred to by a number of writers under the name of pseudobronchiectasis (Jackson) and reversible bronchiectasis (Lander and Davidson,[18] Fleischner[11]). If it can be established that the condition mentioned is definitely clinical bronchiectasis then our entire concept of the disease must be revised. It would no longer be proper to refer to bronchiectasis as irreversible; spontaneous, medical, bronchoscopic and even radiation cures could be expected and the postponement of surgical treatment would appear more justifiable. In the present state of our knowledge of this condition the term "pseudobronchiectasis" would appear quite appropriate.

With this consideration of treatment, we have before us the full life story of bronchiectasis. With this knowledge of the disease, its importance can be more readily appreciated. There is little wonder that many have come to regard bronchiectasis as one of the really important diseases of the respiratory tract. It is rapidly assuming an importance equal to that of tuberculosis. While the latter disease is now fairly well understood, its methods of propagation known, its detection and recognition relatively simple and, what is more important, and methods of treatment now so perfected that there is a steady decline in the mortality rate, it can be hoped that this disease soon will be definitely under control. This is not true of bronchiectasis, however. There is yet much to be learned, and until our knowledge of bronchiectasis is more complete, not too much can be hoped for from our present methods of combatting it. It is for this reason that the prevention of bronchiectasis is of such vital importance.

PREVENTION OF BRONCHIECTASIS

Measures for the prevention of bronchiectasis must be based upon a knowledge of its etiology. Thus in discussing prevention a review of the etiological factors concerned becomes essential.

Obviously nothing can be done to prevent the cases of congenital bronchiectasis. However, since these cases are so few in number their clinical significance is relatively negligible.

In the acquired form of bronchiectasis, bronchial infection stands first and foremost among the causes of this condition. This is particularly true in children. Here the laity, particularly mothers, must be made conscious of the seriousness of the common cold and must be educated in the modern methods of cold prevention as far as this is possible. There must be maintenance of child health at the peak of perfection by proper nutrition, with inclusion of all essential food elements and with special consideration of the various vitamins. There must be insistence upon the proper amount of food, rest and sleep, the avoidance of overfatigue, adequate fresh air and sunshine, proper protection against inclement weather and the avoidance of contact with those suffering from acute respiratory tract infec-

tions. Children with colds should be kept away from school. The prompt attention and proper treatment of the common cold by parent and physician will minimize the likelihood of the development of bronchopneumonia. Such education is the responsibility of every practitioner called upon to treat children. The utilization of women's clubs and parent-teachers associations can serve as vehicles for this educational program.

Since the onset of bronchiectasis is so frequently attributed to an attack of influenza, measles or whooping cough, the physician should take every precaution to prevent or to minimize bronchopneumonia occurring as a complication. A more prolonged or more guarded convalescence in these diseases may aid materially in such prevention. Parents too often fail to appreciate the significance of these diseases of childhood and do not heed the warning of the physician concerning complications. Strict adherence to the treatment prescribed must be insisted upon by the attending physician.

While lobar pneumonia may not be one of the most common causes of bronchiectasis, this possibility occurs with sufficient frequency to demand the attention of the clinician. Incomplete resolution of the pneumonic consolidation is far more common than the average physician appreciates. The roentgenologist has ample opportunity to be familiar with this fact. In those institutions in which cases of pneumonia are closely followed by serial roentgenograms of the chest, the roentgenologist has become impressed with the manner in which the roentgen signs of pneumonia lag behind the physical signs. Clinically, the patient may have made a complete recovery, is without physical signs or symptoms and yet on the roentgenogram there remains evidence that resolution is not yet complete. It is usually at this stage that the patient is discharged from the hospital. Presumably these residual roentgen manifestations disappear in the vast majority of cases. Undoubtedly, however, many of these patients return years later with a well established bronchiectasis at the site of the former pneumonia. This accounts for many of the unilateral cases of bronchiectasis. The prophylactic measure here indicated is quite obvious. In all cases of pneumonia of any variety, if the lungs are not clear when the patient is discharged from the hospital he should be required to return for subsequent roentgen studies. If the abnormal signs persist, a bronchoscopic examination should be made and treatment instituted as indicated. In this manner many cases of bronchiectasis could be prevented.

It is realized that the majority of patients with pneumonia are treated at home without the benefit of roentgen studies. As soon as such patients become ambulatory they should be referred for a roentgen examination of the chest. It is surprising the amount of pulmonary disease that would be revealed if such a procedure were adopted as a routine in every case of pneumonia. Not only would a certain amount of bronchiectasis be prevented but other unsuspected and serious pulmonary lesions would come to light such as tuberculosis and bronchogenic cancer which were directly responsible for or erroneously diagnosed as pneumonia. Also early cases of bronchiectasis itself would be detected in time to prevent the serious consequences of this disease.

The argument is valid that many cases of lobar pneumonia in adults are the result rather than the cause of bronchiectasis. This point is often missed by the clinician in treating pneumonia. If roentgen studies were continued in all cases of pneumonia until the lungs were clear, these unsuspected cases of bronchiectasis responsible for attacks of pneumonia would be revealed and immediate treatment could be started rather than postponing such therapy until the diagnosis of bronchiectasis is all too obvious. When a patient with pneumonia gives a history of having had three or four previous attacks, one can be certain that there is some local cause for

this recurrence. All such cases should certainly be followed after recovery from an attack of pneumonia. Many such patients will be found to harbor an unrecognized bronchiectasis.

Regardless of one's opinion as to the relationship of infections of the paranasal sinuses and bronchiectasis, certainly the patient should be given the benefit of the doubt and the disease in the sinuses eradicated if possible. It should be constantly borne in mind that in every acute respiratory tract infection, every part of this tract is involved even though the symptoms are limited specifically to the lungs, trachea or pharynx. It should be remembered that the sinuses are almost certainly involved and some attention should be given to them. This is advice fraught with some danger since the sinuses will not tolerate too enthusiastic and unskilled treatment. Often they are best let alone, since normal sinuses having adequate drainage during an acute respiratory tract infection will usually take care of themselves. However, the sinuses should not be neglected and when obviously involved should receive appropriate treatment. The practitioner who is not too sure of himself about the paranasal sinuses should consult a specialist.

In a chronic sinusitis in which complete eradication of the disease is practically impossible, measures should be taken to minimize the significance of the pathological changes and to prevent acute exacerbations. This is usually a problem for the rhinologist. And particularly is it a problem in the so-called cases of bronchosinusitis which are the ones most likely to develop bronchiectasis. Often little can be done for these patients without a change in climate. They usually do better and often live in comfort in a warm, dry, equable climate such as is to be found in the southwestern part of this country. The problem is not merely a local one and the general health of the patient must be carefully considered.

The fact that a definite relationship between allergy and bronchiectasis has not been fully accepted should not deter the physician from thinking of allergy in his connection. In patients having frequent respiratory tract infections, especially in those in whom the usual measures for combatting such a predisposition have failed, allergy as the underlying cause should be considered. There are those who believe that the predisposition to frequent "colds" is always an allergic manifestation. Thus a consciousness of allergy and active treatment of this phenomenon when found can, in the present state of our knowledge, be regarded as measures in the prevention of bronchiectasis. In frank cases of hay fever and asthma, the measures taken to combat these conditions automatically act prophylactically against bronchiectasis.

Bronchial obstruction is the other important factor to be considered in acquired bronchiectasis. Such obstruction may arise from something within the lumen of the bronchus. Foreign bodies either radiopaque or non-opaque, are common examples of this kind. All too often the inhalation of a foreign body is too lightly regarded by both the patient and his physician. The absence of symptoms leads to the conclusion that the foreign body has entered the alimentary tract and that nothing, therefore, need be done about it. After an initial period of gagging and coughing, a patient with a foreign body in a bronchus or in the pulmonary tissues may become symptomless. If neglected it is certain to give rise to infection and usually terminates in a localized bronchiectasis. In every instance of foreign body a careful roentgen examination of the neck, chest and abdomen is indicated. Because a foreign body is known to be non-opaque, many physicians believe that a roentgen study is useless. Non-opaque foreign bodies, as a rule, are quite readily detected in the respiratory tract and in the esophagus. Too many physicians are inclined to belittle the importance of the swallowing of a foreign body and often roentgen studies are done upon the insistence of the patient. The roentgen examination should be carried out as soon after the inhalation of the foreign body as is

practical. The damage done by a foreign body in the lung is, in a measure, dependent upon the duration of its sojourn and should therefore be removed at the earliest possible moment.

The problem of foreign bodies in the respiratory tract is particularly important in the case of children. In such patients, a history is often lacking, due to the fact that in infants no one may have seen the child swallow a foreign body and in the case of older children they are often afraid to tell of such an incident. Such cases are fairly common in roentgenological practice, and unfortunately many such patients do not reach the roentgenologist for months or years after the aspiration of a foreign object. By this time a bronchiectasis has usually become well established. In a child having repeated respiratory tract infections or in one already showing symptoms suspicious of bronchiectasis the possibility of a foreign body should be considered. In such cases a careful roentgen study should be carried out and in the event of a negative report a bronchoscopic examination should be done to absolutely rule out the presence of a foreign body.

In small children having persistent symptoms of coryza and nasal discharge a roentgen examination of the paranasal sinuses should be made. Very occasionally one will find a foreign body such as a bean, button or a wad of paper in one of the nasal chambers which the youngster has pushed up into the nose.

Broncholiths act in much the same manner as extraneous foreign bodies in producing bronchiectasis. So little is known regarding the etiology of these calcareous deposits in the lung that little or nothing can be said regarding their prevention. Fortunately broncholiths as a cause of bronchiectasis is apparently not of common occurrence and the relationship, therefore, is of more or less academic interest.

Occluding secretions within a bronchus resulting in bronchiectasis are of considerable clinical importance. Probably the best known example of this kind is postoperative atelectasis. Bronchial occlusion by secretions may also occur in pneumonia, during an attack of asthma or in the newborn from the aspiration of mucus or meconium. While the resultant atelectasis in these conditions can often be suspected clinically, roentgen examination is usually required for confirmation of the diagnosis.

Prophylactic measures for postoperative atelectasis are, at the same time, preventives of bronchiectasis. Frequent change in the position of the patient after operation, the avoidance of excessive sedation which tends to suppress the cough reflex and the stimulation of respiration by carbon dioxide inhalations are measures which have been successfully used to prevent this type of atelectasis. If the atelectasis does not clear promptly bronchoscopic aspirations should be resorted to.

In the presence of atelectasis due to occluding secretions of whatever origin, prompt removal of the secretions by means of the bronchoscope should be carried out. When the roentgenogram in pneumonia indicates a definite atelectasis bronchoscopic aspirations should be considered, provided this procedure is not contraindicated by the patient's condition. In the newborn direct suction by way of the upper respiratory tract will usually be sufficient to dislodge the obstructing material.

Bronchial obstruction may result from a lesion having its origin in the wall of the bronchus itself. In this category are strictures which may be either traumatic or infectious in origin. A traumatic stenosis may result from lodgment of a foreign body or from attempts at its removal. Thus great skill and care must be exercised in the bronchosopic removal of foreign bodies. Prevention has already been considered for strictures resulting from bronchial infection. In stenosis of specific origin, such as occurs in tuberculosis and syphilis, the primary disease is usually more important than any complicating bronchiectasis. The same holds true for the extensive pulmonary fibrosis occurring in tuberculosis and pneumoconiosis. Bronchiectasis oc-

curring under such conditions is usually of secondary importance.

We may here consider all forms of tumors regardless of whether they arise from the wall of a bronchus or press upon the bronchus from without. Such lesions are of frequent occurrence and the malignant varieties are increasing in incidence. There is, of course, no known means of preventing neoplasms. Much, however, can be done for benign adenomata which are much more frequent than generally supposed. Roentgenologically, it is not possible to distinguish between the benign and malignant bronchial neoplasm. All such cases should have a biopsy taken from the tumor by the bronchoscopist. Often the entire tumor can be removed bronchoscopically with complete cure. When this cannot be done and the tumor is histopathologically benign a cure can be obtained by lobectomy. Simply because the vast majority of bronchial tumors are malignant should not lead one to the conclusion that all of them are malignant. Occasionally such tumors are not neoplasms at all but granulation tissue from various causes. Here again the bronchus can be relieved of its obstruction by the bronchoscopist and bronchiectasis prevented.

Bronchial obstruction may occur as the result of pressure extrinsic to the bronchus itself. Enlarged lymph nodes usually result from pulmonary infections the prevention of which has already been discussed. Tuberculosis is a common cause of hilar lymph node enlargements. The prophylaxis of this condition is common knowledge and need not be considered here. Enlarged lymph nodes of malignant origin either primary or secondary and those resulting from the various lymphoblastomata cannot be prevented.

The prevention of bronchiectasis due to pulmonary fibrosis means the prevention of the cause of the fibrosis. The fibrosis of pulmonary tuberculosis has already been discussed. In the fibrosis of pneumoconiosis much has already been accomplished in the prevention of the inhalation of harmful dusts and such efforts are being continued by those interested in this important pulmonary disease. Other types of pulmonary fibrosis are usually of infectious origin and prophylactic measures must be directed toward the prevention of these specific infections.

Finally, under the heading of miscellaneous causes of bronchiectasis are lesions of the pleura and of the thoracic cage. Such conditions are usually secondary so that preventive measures must be directed toward the primary condition. Since these are so varied and numerous and since bronchiectasis from such causes is not of frequent occurrence, an attempt to discuss prevention in this group of cases would serve no useful purpose.

In general, it may be said that two of the most useful and important procedures in the prevention of bronchiectasis are the roentgen examination of the chest and the bronchoscopic examination. In every affection of the respiratory tract in which symptoms are persistent or do not readily respond to treatment, a roentgen examination is indicated, including the sinuses as well as the chest. This will frequently reveal conditions which, if promptly taken care of, will prevent the development of bronchiectasis. This type of examination is now generally available to everyone regardless of how small the community.

More frequent use of the bronchoscope in persistent disease of the respiratory tract would do much toward preventing bronchiectasis by the early detection of those conditions known to give rise to bronchiectasis. Unfortunately this type of examination is not as generally available as might be desired. Adequately trained men in this specialty are still scarce. It is unwise to entrust a patient to a physician who has not been thoroughly trained in this field. It is far better for the practitioner to send his patient to one of the many clinics where expert bronchoscopy is available.

Finally, in the prevention of bronchiectasis an educational program for both the laity and the medical profession is a matter

of prime importance. Laymen must be told and impressed with possible seriousness of the common cold, especially in children. They must be taught the very simple preventive measures available to all. They must have impressed upon them the necessity of seeking medical attention when suffering from repeated respiratory tract infections or when such an infection persists and does not readily respond to the usual remedies. Much can be done in the education of parents regarding the dangers of foreign bodies gaining access to the respiratory and alimentary tracts. In an analysis of 1,135 cases of foreign body in the air and food passages, Jackson and Jackson[17] came to the conclusion that carelessness was responsible for 87 per cent of the cases. Here is a fertile field for education and preventive efforts. Such educational efforts will fall largely to the lot of the general practitioner, the pediatrician and the otolaryngologist who see patients when the etiological factors of bronchiectasis are at work and at a stage when bronchiectasis can be prevented.

Of greater importance at the moment is the education of the medical profession itself. There are so many physicians who know so little about bronchiectasis. There are many others to whom the thought of the prevention of bronchiectasis has never occurred. Physicians must be disabused of the idea that nothing can be done to prevent bronchiectasis. A clearer knowledge of the entire problem of this disease, particularly its etiology and economic importance, will do much to arouse interest of the general medical profession. This educational program must include the roentgenologist because there are many such specialists who do not have the true concept of bronchiectasis and the problem it presents.

In this educational program the roentgenologist has an excellent opportunity to render real service. As has already been stated, he has an opportunity to view the entire life history of bronchiectasis from the etiological stage to the terminal events. He can educate his colleagues regarding many of the pertinent facts of bronchiectasis, he can direct their attention to the possibility of a developing or the existence of an early bronchiectasis, and finally he can suggest a bronchoscopic examination when in his opinion this procedure is indicated. Thus, in the prevention of bronchiectasis, a roentgenologist who is conscious of and has a full knowledge of this disease is an asset of prime importance.

REFERENCES

1. Berck, M. Radiotherapy for bronchorrhea in bronchiectasis. *J. Mt. Sinai Hosp.*, 1934, *1*, 98–100.
2. Berck, M., and Harris, W. Roentgen therapy for bronchiectasis. *J. Am. M. Ass.*, 1937, *108*, 517–522.
3. Boyd, W. The Pathology of Internal Medicine. Lea & Febiger, Philadelphia, 1936, p. 181.
4. Bradshaw, H. H. Personal communication.
5. Bradshaw, H. H., Putney, F. J., and Clerf, L. H. Fate of patients with untreated bronchiectasis. *J. Am. M. Ass.*, 1941, *116*, 2561–2563.
6. Clerf, L. H. Interrelationship of sinus disease and bronchiectasis with special reference to prognosis. *Laryngoscope*, 1934, *44*, 568–571.
7. Diamond, S., and Van Loon, E. L. Bronchiectasis in childhood. *J. Am. M. Ass.*, 1942, *118*, 771–778.
8. Duken, J., and von den Steinen, R. Das Krankheitsbild der Bronchiektasis im Kindesalter. *Ergebn. d. inn. Med. u. Kinderh.*, 1928, *34*, 457–466.
9. Erb, I. H. Pathology of bronchiectasis. *Arch. Path.*, 1933, *15*, 357–386.
10. Farrell, J. T., Jr. Importance of early diagnosis in bronchiectasis; clinical and roentgenologic study of 100 cases. *J. Am. M. Ass.*, 1936, *106*, 92–96.
11. Fleischner, F. G. Reversible bronchiectasis. Am. J. Roentgenol. & Rad. Therapy, 1941, *46*, 166–174.
12. Goodale, R. L. Analysis of 75 cases of bronchiectasis from viewpoint of sinus infection. *Ann. Otol., Rhin. & Laryng.*, 1938, *47*, 347–359.
13. Graham, E. A. Observations on reaction of bronchial fistulae to acute infections of upper respiratory tract. *Am. J. Surg.*, 1931, *14*, 382–383.
14. Greey, P. H. Bacteriology of bronchiectasis; analysis based on 9 cases in which lobectomy was done. *J. Infect. Dis.*, 1932, *50*, 203–212.
15. Hamman, L. Bronchiectasis. Oxford University Press, New York, Vol. 11, p. 24.
16. Jackson, C., and Jackson, C. L. Bronchiectatic

septic tank; its prophylaxis and treatment. *Am. Rev. Tuberc.*, 1934, *30*, 599–606.

17. Jackson, C., and Jackson, C. L. Diseases of the Air and Food Passages of Foreign-Body Origin. W. B. Saunders Co., Philadelphia, 1936.
18. Lander, F. P. L., and Davidson, M. Aetiology of bronchiectasis. *Brit. J. Radiol.*, 1938, *11*, 65–89.
19. Leopold, S. S. Bronchiectasis; medical aspects. *Arch. Otolaryng.*, 1941, *34*, 966–973.
20. Perry, K. M. A., and King, D. S. Bronchiectasis; study of prognosis based on a follow-up of 400 patients. *Am. Rev. Tuberc.*, 1940, *41*, 531–548.
21. Raia, Antoinette. Bronchiectasis in children, with special reference to prevention and early diagnosis. *Am. J. Dis. Child.*, 1938, *56*, 852–882.
22. Roles, F. C., and Todd, G. S. Bronchiectasis; diagnosis and prognosis in relation to treatment. *Brit. M. J.*, 1933, *2*, 639–643.
23. Smith, D. T. Etiology of primary bronchiectasis. *Arch. Surg.*, 1930, *21*, 1173–1187.
24. Warner, W. P. Factors causing bronchiectasis; their clinical application to diagnosis and treatment. *J. Am. M. Ass.*, 1935, *105*, 1666–1670.
25. Watson, S. H., and Kibler, C. S. Rôle of allergy in bronchiectasis. *J. Allergy*, 1939, *10*, 364–376.

Vol. 51, No. 3

PULMONARY AND OSSEOUS MANIFESTATIONS OF TUBEROUS SCLEROSIS, WITH SOME REMARKS ON THEIR PATHOGENESIS*

By ALFRED J. ACKERMANN, M.D.
OKLAHOMA CITY, OKLAHOMA

THE protean character of tuberous sclerosis and other ectodermoses makes difficult a satisfactory comprehension of the pathologic process involved. The true nature of some manifestations encountered in this disease, especially in its "form fruste," may remain unrecognized by the clinician, and be misinterpreted by the roentgenologist, unless they are familiar with the relation of these disorders to the ectodermoses. It may therefore not be amiss to report a case studied at the University Hospital, and raise some questions, which, then considered on a larger material, may throw additional light on our knowledge of this interesting syndrome.

CASE REPORT

V.G. (Hosp. No. 77335), white male, aged twenty-five, was admitted to the University Hospital in October, 1934, complaining of polyuria, nocturia, pain in the chest, back and in both legs. For the last two years previous to admission, the patient has been drinking large quantities of water, and correspondingly his urine output has averaged approximately 10 liters daily. The patient had no headaches or visual disturbance. The pain in the chest was dull; patient coughed occasionally, but raised no sputum, and had no hemoptysis. The temperature was apparently normal. The pain in the back and legs seemed to be of muscular character, more intense at night and in the morning, with some improvement after moderate exercise. Because of definite pulmonary pathologic condition, revealed by roentgen examination, the patient was for some time under observation in a tuberculosis sanatorium, but discharged without advice to continue treatment when repeated sputum examinations failed to reveal tubercle bacilli.

On physical examination the patient appeared older than his age; all teeth were absent; no abnormal findings were elicited within the chest or other internal organs. The skin was dry, slightly atrophic, without any abnormal pigmentation.

Roentgen examination of the chest showed an irregular honeycomb pattern, with numerous multangular areas of increased translucency, varying somewhat in size, and separated from each other by rather thick fibrous strands, which formed a nodular arrangement at points of their intersection. There were larger thin walled cystic cavities in the right lung field, without demonstrable fluid levels. The mediastinum was free. There was no displacement of the cardiac shadow toward either side.

Roentgenograms of the maxilla and mandible were reported to have shown a complete absence of teeth, and marked decalcification of these bones, which was suggestive of disturbed calcium metabolism. The remainder of the skeleton was not examined at that time.

After three weeks of observation the patient was discharged, but returned shortly thereafter, stating that one week after his dismissal he had had severe pain throughout the left chest and severe dyspnea. The pain has continued, and the patient was raising large amounts of watery material.

On physical examination signs of pneumothorax and mediastinal displacement were elicited. Otherwise the patient presented the same features as on the previous examination.

Roentgen examination of the chest showed pneumothorax of the left pleural cavity, with marked collapse of the left lung, and a contralateral displacement of the heart and mediastinum. There were no structural changes within the lungs not seen on the original examination. A roentgen diagnosis of polycystic lung disease with pneumothorax subsequent to a rupture of one or more of the small cysts was made.

The patient remained under clinical observation, in the course of which the skeleton was examined roentgenologically, and the blood chemistry was studied.

* From the X-Ray Department of the State University and Crippled Children's Hospitals (John E. Heatley, M.D., Director)

Fig. 1. Both lung fields show a honeycomb pattern with numerous multangular areas of increased translucency, separated by thickened fibrous strands.

Roentgenograms of the vertebral column showed an asymmetry of the body of the first lumbar vertebra, whose left lateral margin was slightly excavated. On the lateral view there was a fairly large erosion of the anterior portion of the vertebral body. The bone adjacent to this erosion was moderately sclerotic. Both vertebral plates were preserved. Within both iliac bones there were several large, sharply defined areas of rarefaction, varying considerably in size and shape. The adjacent bone trabeculae were of increased density, coarse and somewhat irregularly arranged. The medial portion of the wing of the left iliac bone, near the sacroiliac articulation showed numerous smaller cyst-like areas of decreased density, with definite evidence of confluence of several of these cysts. There were similar areas of rarefaction within the right pubic bone, extending even beyond the cortical portion of the bone. A few fairly large bone spicules extended from the pubic bone toward the foramen obturatum. Both femoral necks and the juxtatrochanteric portions of the shaft showed numerous cystic areas, varying in size from that of a hazel nut to that of a large hen's egg. Surrounding these rarefactions was usually a narrow zone of sclerotic bone. The shafts showed slight expansion at the sites of the cystic cavities. The diaphyses of both femora showed a diffuse fibrillation of the cancellous bone, with some thickening of the bone trabeculae, which were fairly separated by fusiform areas of rarefaction. The cortex remained intact.

The blood count showed no deviation from normal. The blood calcium was 9.8 mg. per 100 cc.; phosphorus 4.2 mg., phosphates 3.56 mg. The nonprotein nitrogen was 35 mg., uric acid 3.5 mg., blood sugar 80 mg., and cholesterol 133 mg. per 100 cc. The daily amount of calcium excreted in the urine on a calcium free diet was 528 mg.

In May, 1940, the patient was readmitted to the hospital. At this time he complained of polydypsia, polyuria and pain in the back and both lower extremities. He had no complaints referable to the chest.

In addition to the findings previously mentioned, there was marked muscular atrophy, especially of the lower extremities; flexion contracture of 10 to 15° of both thighs and flexion contracture of 10° of the right knee, and 20° of the left knee. There was some tenderness over the right thigh posteriorly, close to the

Fig. 2. Pneumothorax reveals numerous small subpleural cysts.

greater trochanter. The spine showed a marked prominence and slight right scoliosis of the twelfth dorsal and first and second lumbar vertebrae. There was some tenderness over this segment of the spinal column.

A re-examination of the skeleton and chest showed no appreciable progress of the pathological changes within this period of time.

From the patient's history and clinical findings, it was obvious that he presented a definite diabetes insipidus, polycystic lung, and a certain form of multiple osteodystrophy.

In absence of signs of an endocranial tumor over an eight year period of observation, it seemed safe to conclude that the diabetes insipidus was not caued by a neoplasm of the pituitary body. The blood chemistry did not support a possible diagnosis of osteitis fibrosa cystica due to hyperarthyroidism. The blood calcium and phorphorus level were found normal. The pulmonary pathologic condition exhibited by the patient was of great interest *per se*.

Attempting to reduce these various clinical complexes to one common etiological factor, we considered the possibility of Schüller-Christian's disease, a systemic disorder in which diabetes insipidus and skeletal alterations are the outstanding features of the disease. Although involvement of the lung is extremely rare, there are known cases of generalized xanthomatosis with miliary dissemination in the lungs. We were unable to find sufficient evidence to warrant this diagnosis in our case. The characteristic cranial defects were absent; there was no demonstrable disturbance of the lipoid metabolism.

Fig. 3. Basal portion of the right lung demonstrating the detail of the pulmonary pattern.

Fig. 4. The lateral margin of the first lumbar vertebra is excavated.

Tuberous sclerosis seemed to us to be the only disease which could explain the manifold symptoms presented by the patient, and account for the patho-anatomical changes in such divergent organs as brain, lung and skeleton.

According to our present conception, tuberous sclerosis is a form of congenital ectodermoses, which in addition include three other outstanding entities: (1) von Recklinghausen's neurofibromatosis; (2) anginomatosis cerebri, and (3) Hippel-Lindau's disease.

A complete discussion of the clinical manifestations of tuberous sclerosis would exceed the scope of this presentation, and we refer to the literature on this subject.

Fig. 5. Lateral view of the first lumbar vertebra shows an erosion of the vertebral body and sclerosis of bone adjacent to it.

In fully developed cases one finds most frequently the following symptoms: (1) epileptic seizures (genuine or jacksonian); (2) mental deficiency; (3) cutaneous lesions, known as adenoma sebaceum, and (4) congenital tumors of the eye and many visceral organs (rhabdomyoma, hypernephroma, renal lipomyosarcoma, tumors of the spleen, lymph nodes, lungs, retina and bones).

Clinical manifestations of the disease, when fully developed, appear rather early and are often recognizable in infancy. The protean character of the disease, which may in some instances present only certain of its characteristic features, quite frequently precludes an early diagnosis unless one is aware of its symptomatology. Many patients afflicted with this disease may present only abortive manifestations, which sometimes become apparent in the later decades of life. Cases in the sixth and seventh decades of life have been reported. The clinical symptoms depend on the organs involved. In some cases the endocranial lesions dominate the clinical picture, in others the visceral tumefactions are responsible for the patient's complaints.

Pathologically, tuberous sclerosis is characterized by the presence of potato-like tumors, varying in size from 0.5 to 3.0 cm. in diameter. These tumors occur most frequently in the cerebral hemispheres, although other parts of the central nervous system may also be involved. In the walls of the third and the lateral ventricles, immediately beneath the ependyma, small irregular projections are found, arising usually from the thalamus. These appear as tiny, button-like tumors, or when larger in size as "candle-gutterings" (Lind) running from above downward and following the tributaries of the vein of the corpus striatum. Although macroscopically the tubera seem to be sharply demarcated, there is no abrupt transition between normal and diseased tissue, when studied microscopically.

The microscopic alterations characteristic of tuberous sclerosis affect the pyramidal cells and the glia. The pyramidal cells may be present in the more superficial layers, and granular elements may be scattered among the larger neurones of the deeper parts. The orientation of the pyram-

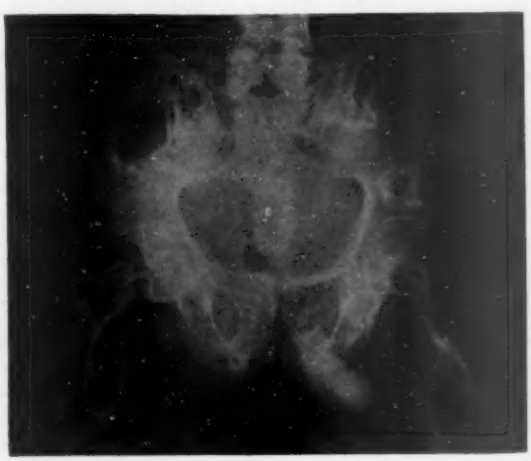


Fig. 6. Numerous cystic areas within the iliac, ischial and pubic bones and both femora.

idal cells may be altered so that these cells assume an abnormal polarity. The morphological state of many of the cells is changed. There may be a clumping and later disappearance of Nissl granules; the nucleus may assume a lateral position. The process may become thicker, and the cells as a whole may skrink.

The neuroglia exhibits marked proliferation. There is a considerable overgrowth of glial fibrils which are mainly of the thin type. The proliferation occurs primarily within the cortex, though it extends for some distance into the underlying white matter. One finds peculiar interlacing of the fibers. In the subependymal growths the neuroglial proliferation produces a loosely interlacing complex of parallel strands. The ependymal covering remains intact, and between this layer and the glial overgrowth is an interval occupied by loose areolar tissue. In the intraventricular growths the glial proliferation may become excessive and give rise to definite, macroscopically discernible tumors.

Fig. 7. Detail view of the left femur shows multiple, partly confluent cysts.

Fig. 8. Detail view of the cystic changes and associated sclerosis of the right femur.

Great significance has been attached to the giant cells within the foci of tuberous sclerosis. Since Harthagen's original description they have been noted by all writers concerned with this subject, and have caused much discussion as to their nature and their bearing upon the conception of tuberous sclerosis in general.

These cells lie typically in the depth of the sclerotic nodules, i.e., where the neuronic and glial changes are most intense.

Fig. 9. Shaft of the femur, showing fibrillation of the cancellous bone and fusiform areas of rarefaction.

Both cortical and subependymal tubera may contain such cells, though they are more numerous in the former situation. It is important to realize that they may occur outside of the cerebral cortex; thus they appear as heterotopies in the white matter near the tubera. Furthermore, they may be demonstrable in the cortex away from the sclerotic regions, and they have also been noted in more remote portions of the nervous system such as the cerebellum, medulla, and spinal cord.

Much controversy has arisen as to the nature of these large cells, and in particular as to whether they are derivatives of glial or nerve elements. It appears definite from careful histopathological studies that all the large cells of a particular case do not have the same morphological and staining characteristics and probably represent entirely different cells, their sole common feature being their large size.

A large cell of neuronic type and a large cell with glial resemblance are distinguished.

The large cells usually predominate slightly and are more numerous in the cortical than in the subependymal growths. They are well demonstrated by the ordinary nerve cell stains and particularly by Bielschowsky's method. They do not react to glial stains. They vary in size from a large pyramidal cell up to that of a Betz ganglion cell; and when secondary changes occur, further distention may increase their bulk still more. As a rule, they occur in clusters of three or more and may be surrounded by some densification of the glia. They are occasionally triangular in outline but the larger specimens are elliptical or even circular.

The internal structure of these cells shows various abnormalities in the position and staining reactions of the nuclei. Considerable variability exists in the character of the process; sometimes they are short and thick, and at times a stem arises which quickly breaks up into finer branches. The neuronic character of this type of cell is suggested by the presence of intracellular fibrillary network and also of Nissl granules.

The large cells with glial resemblance are somewhat less numerous and occur more particularly in the ventricular nodules. They are also grouped in the vicinity of blood vessels, to the walls of which they may be attached. Their shape in unlike that of a nerve cell, being oval or circular. There are no intracellular fibrils or granules, and the processes are invisible except in silver stained preparations. With such methods the processes are displayed, sometimes recalling those of a nerve cell, but at other times numerous short and curly processes radiate at intervals from the periphery.

Histopathological studies of other organs, frequently affected by the pathologic process, underlying tuberous sclerosis and allied conditions, have been extensively reported in the medical literature. Only

observations regarding pulmonary and skeletal involvement are very scant.

Berg and Vejlens observed 3 cases of tuberous sclerosis with pulmonary manifestations, 2 of which occurred in members of the same family. One of these cases has been studied by them anatomo-pathologically and we should like to quote the description of their findings:

The lungs presented a unique appearance. They had everywhere, except laterally at the right tip, grown on the wall of the thorax by means of rather loose connective adherences. The free space corresponded to a pneumothorax cavity of the dimension of a good sized tangerine, the existence of the cavity having been previously proved roentgenologically. The lungs were large and voluminous and felt to be more air-cushioned than usual. The surfaces were dotted with small air fitted bubbles, not more than pea size, suggesting a bullous emphysema. The walls between the larger cysts often reached 0.5 cm. in thickness, but they contained a number of miniature cysts. In places the cyst walls were only the thickness of paper and had been perforated.

Microscopically the walls of the cyst consisted to a large extent of connective tissue containing numerous blood vessels. But the most salient component was plain muscular tissue. This muscular tissue moreover was not, as in the description of cystic lung previously given by Buchmann and Oudendal and others, disposed in thin, superficially parallel layers. Nor did it bear resemblance to the more irregular muscular proliferations of von Steussel's muscular cirrhosis of the lung. It had the unmistakable character of tumor tissue, a fact which differentiates the present "cystic lung" from all other cases described hitherto. The nuclei of the muscular fibers were in the main somewhat broader than usual. Further the contractile substance, which is stained yellow in the normal way by picric acid, according to van Gieson's method, had not always the same regular, narrow, fusiform shape, which is so characteristic of the smooth musculature. The muscular fibers were often shorter and thicker and blunted at the ends. They are probably to be regarded as survivals from the embryonic stage, without however presenting the appearance of malignant tumor cells. The essential characteristic of this myomatous tissue was that the muscle fibers were joined together in intercrossing bunches and clusters, precisely as in the case of ordinary myoma, and in the same way as in the tumor-like formations in the kidney, for example. The lungs presented, apart from the general cystic transformation, the aspect of a diffuse myomatosis, which must be considered as very closely related to the genuine tumor formation.

It is doubtful whether the lung cysts in tuberous sclerosis should per se be characterized as malformation, and if one knows that sclerotuberous alterations were established in the brain and the kidneys, as usual, and were also found in a single lymphatic gland and in the spleen, and if, further, due regard is paid to the fact that the disease is of familial character, then one is justified, it would seem, in holding that the myomatous changes in the lung tissue are also an expression of a general malformational disease with a tendency towards tumor formation.

Roentgen studies of these cases were reported by Berg and Zachrisson, and they conform with those observed in our case. These authors emphasized the irregular, honeycomb-like pattern made up of scarcely visible to hazel nut sized translucencies, separated by fine, round striae, noticed in both lung fields. These markings seemed to become less dense at the apex, where the cavities were of larger size. The points of intersection in the honeycomb structure did not show any particular tendency to mottling, although the appearance on the whole resembled that seen in different forms of miliary dissemination.

They discussed the differential characteristics between the tuberous sclerosis and other miliary disseminations.

Skeletal involvement in cases of tuberous sclerosis has been reported by Gottlieb and Lavine, Kveim, and Heublein, Pendergrass and Widmann.

The histopathological alterations of the skeleton have been described by Kveim, according to whom "in the decalcified sections one finds cancellous bone, with thick bone trabeculae. The bone architecture is

irregular; it looks more like cartilage and shows a poor calcium content. Few cells are visible within the marrow spaces of the bone; instead one encounters, scattered here and there, diffuse, fibrous tissue, poor in cells. No signs of inflammation or tumor formation are present. From the periosteum toward the bone one finds nearly homogeneous, hyalinized connective tissue clumps and masses. Though signs of inflammation are absent, the marrow shows isolated areas, resembling osteitis fibrosa."

The roentgenological findings observed within the skeleton by these authors show a marked similarity.

Gottlieb and Lavine found periosteal thickening and generalized fibrosis of metatarsal and metacarpal bones and their associated phalanges. There was also a generalized fragmentation of the cortical layers. Several of the bones of the hands showed areas of marked rarefaction, suggesting small cysts. The bones of the cranium showed a peculiar mottling, with indistinct islands of increased density alternating with areas of rarefaction throughout the bone. Both the internal and external tables appeared thicker and denser than normal.

Kveim reported in his cases the presence of similar changes affecting the cranial bones. The bones of the hands showed periosteal thickening, sclerosis and centrally located areas of rarefaction within the phalanges and metacarpals. The skeletal changes resembled those of osteitis fibrosa.

The presence of tumors and other disorders within organs derived from the mesoderm, associated with tuberous sclerosis, which is preëminently a disorder of the ectodermal layer, caused numerous theories to be advanced, which attempted to place all these disorders on a common basis.

Bielschowsky was of the opinion that the presence of cutaneous and visceral lesions in close association with tuberous sclerosis was of utmost importance. All of these alterations, in his view, could and should be reduced to congenital, or even better, embryonal developmental disturbances. The manifestations of this disturbance are not uniform. Whereas in one organ the element of developmental inhibition predominates, in other organs are observed enormous new formations, which apparently have their origin in a faulty blastomatous developmental tendency of some tissue components. These changes occur most likely in early embryonal life, but they do not terminate with birth. A formation of new foci probably does not occur in extra-uterine life. The preformed foci are, however, capable of further growth.

Kveim thought that none of the ectodermoses is a genuine neoplasm, but that the condition is due to anomalies of fetal differentiation, so-called "embryo-plasmatic dysplasias," which chiefly attack the ectoderm—first and foremost the neural plate—at a very early stage. Kveim also considered a possible genetic connection with Recklinghausen's neurofibromatosis, in which he assumed that there also exists a fetal dysplasia of the ectoderm-mesoderm (the neural plate?). While the cell elements affected here are essentially those which form the origin of the sheaths of Schwann, so that neurinomas are localized in the peripheral nervous system ("spongioblastosis peripherica"), the cell elements chiefly impaired by tuberous sclerosis are those which in the fully grown individual are localized in the central nervous system ("spongioblastosis centralis"). Kveim explained the occurrence of tumors derived from mesodermal structures on the basis of polyvalent possibilities of differentiation of all cells at a very early stage of fetal life. The connective tissue elements may therefore be looked upon as originating from the same cell elements as the epithelial part of the tumor. The dysplastic cells are characterized by retarded differentiation.

With regard to the multifarious tumors, consisting partly of cells, difficult to classify, occurring in the internal organs, derived from the mesoderm, he states that these have developed by the same "embryoplastic dysplasia," certain cell elements having been attacked before any differen-

tiation of the blastula into the ectoderm and mesoderm has taken place. The several strange cell forms of these tumors may indicate also a kind of subsequent differentiation process.

Worster-Drought, Dickson, and McMenemey also turn to changes effected in early embryonal life for an explanation of the occurrence of ectodermal and mesodermal tumors in any of the neurocutaneous syndromes. They call attention to the experimental work of Needham, Waddington, and their associates on the so-called "embryonic induction." According to this hypothesis "evocator substances" are released by the nerve fibers, which call forth normally a parallel arrangement of the Schwann cells and the orderly distribution of the adjacent mesodermal supporting tissues. Any derangement affecting the nerve elements (ectoderm) and, therefore, the evocator substance, may gravely influence the surrounding mesoblast, producing such changes as are encountered in neurofibromas, multiple meningiomas, etc.

Gottlieb and Lavine, Kveim, and Yakovlev attributed the skeletal changes to the developmental disorder of the mesoderm, and Yakovlev, in view of the accepted affinity of tuberous sclerosis and neurofibromatosis, considered the possibility that the cystic cavities within the bones may be due to true Schwann cells arising from the periosteal nerves, and destroying the neighboring bone by pressure rather than invasion.

A close study of the osseous changes in tuberous sclerosis reveals that they are not uniform. One finds bone sclerosis, periosteal thickening, bone rarefaction, and cyst formation. Very few of the cysts could be classified as of subperiosteal origin, and one does not find the sharp line of demarcation usually associated with pressure erosion.

The histopathological changes, resembling those of osteitis fibrosa cystica, do not contribute to our understanding of them, since this histopathological picture is a too frequent response of bone marrow to different damages and stimuli. It may occur in a number of essentially different bone diseases, such as inflammatory, neoplastic, metabolic and simple mechanical disturbances, so that the histopathological diagnosis of osteitis fibrosa quite often may, in the special case, be more obscuring than revealing. In a great number of cases, it is only a symptomatic and not a nosologic diagnosis.

The pathogenesis of the skeletal changes in tuberous sclerosis, and possibly also in neurofibromatosis, may perhaps be better understood if one associates them with those in the central nervous system and sees in them an expression of physiopathological disturbance rather than of embryonal tissue dysplasia.

The cases exhibiting skeletal changes showed the tubera to be located in the floor of the lateral ventricles and within the third ventricle. In other words, the lesions involved the thalamic and hypothalamic area of the brain. We may also assume that in our case the diabetes insipidus was due to involvement of this area.

The significance of the hypothalamus in skeletal disorders has recently been emphasized by Lichtwitz, who in a discussion of bone pathology of hypothalamic origin states:

> Although no case has been reported in which such a central nervous lesion [destructive processes in the hypothalamus] produced precocious sex maturation and cystic osteopathy simultaneously, there is sufficient evidence to prove that bone disorders develop following encephalitis. . . . The history of a man, who at the age of 41, fell ill with a grippe which was characterized by sleep inversion, is of particular interest in this connection. After the illness, he developed the following features: diabetes mellitus, hepatosplenomegaly, atrophy of the gonads, arthritis and a generalized osteoporosis with many large cysts in both humeri and femurs. . . . Spontaneous fractures occurred repeatedly. For the last 2 years the bone disorder has remained stationary. A blood chemistry at this time showed 10.6 milligrams per cent calcium and 2.0 phosphorus . . . .
>
> In this case a hypothalamic lesion brought on —beside other disorders—cystic bone disease. . . . As regards the parathyrotropic hor-

mone, increased or diminished production may follow a central nervous disorder. Thus, hypophysectomy in dogs and rats is followed by regressive changes in the parathyroids (P. E. Smith, S. Koster and A. Geesink) and in the toad leads to hypocalcemia (H. A. Shapiro and H. Zwarenstein). These facts throw light on the following observations: A woman, 52 years of age, with long-standing diabetes insipidus, developed signs of Simmonds' disease and a hypocalcemic tetany; a man, 38 years of age, having suffered repeated head injuries by beating, developed a chronic brain lesion, revealed by pneumencepahlography as atrophy and hypocalcemic tetany.

The cases of precocious puberty with osteopathy lack all evidence of an increased production of parathyrotropic hormone and of parathyroid hyperactivity. There seems no other way in which to interpret their mechanism than to assume that the hypothalamic lesion, while provoking other phenomena via the anterior pituitary, increases the sensitivity to the normally produced parathyroid hormone.

The influences emanating from the central nervous system and particularly from the hypothalamus determine the hypersensitivity as well as the resistance of the effector organs. If a pathologically increased quantity of hormone is taken up by more susceptible, but dimensionally limited areas of the bony substance, a stormy reaction will set in, with large amount of lime salts released and with vehement local changes, which lead to the development of 'brown tumors'. When the same quantity of hormone is distributed over the entire skeleton the resultant pathologic changes will develop more slowly, and will be less intense. . . . In analyzing the findings one must consider that the osteopathy, irrespective of whether the disease leads to cyst formation or to generalized osteoporosis, does not, as a rule, advance steadily. There are periods during which the cystic osteopathy is arrested and remains stationary, so that at times the blood calcium level is found to be normal or only slightly elevated.

Perhaps not the neuro-endocrine factor alone may be responsible for the bone changes, which resemble somewhat those described by Freund in osteodystrophia fibrosa unilateralis.

Freund refers in his article to the experimental work of Bentzon and concludes that these skeletal changes may be due to a disturbance in the innervation of the vessels. They would then represent a reaction to active hyperemia of bone tissue. The hyperemia is due to anomalies in the vegetative nervous system, followed by paresis of the muscles of the vessels with vascular dilatation. It may well be that the neurovascular changes play an important part in producing fibrous dystrophies of bone.

The consideration of the pathophysiological aspect rather than the anatomopathological aspect alone seems to us to be of great importance. We so often look upon the mature skeleton as a static organ and lose sight of the anabolic and catabolic processes taking place within the bones. These processes are dependent upon neuroendocrine and neurovascular influences through a mechanism of mutual correlation. The activity of the parathyroid glands is controlled by the parathyrotropic hormone, the production and discharge of which is linked to the metabolism of calcium and phosphates. The parathyrotropic hormone does not seem to be released directly, but is stimulated through the hypothalamic center, which is specifically sensitive to calcium and phosphate concentrations. On the other hand, a lesion within the hypothalamus may increase the tissue sensitivity to normally produced parathyroid hormone. If anomalies of the vegetative nervous system cause also paresis of the muscles of the vessels and vascular dilatation, then the metabolic process within the bone is even more impaired. As a result of these abnormal functional phenomena, the bones show marked alterations of their anatomical structure. Because of the histopathological picture of fibrosis, they are classified as fibrodystrophies.

We have presented these views regarding bone changes in tuberous sclerosis because they offer a functional explanation of the involved process, and may form an important link in the understanding of other bone dysplasias in which one does not find an obvious disturbance of the metabolism of calcium and phosphates. Whether or not

this conception can be sustained will depend largely on observations made on a larger material of the same type.

Concerning the pulmonary alterations we are unable to offer any original views, and hold with the other authors that they are an inherent manifestation of the basic disorder underlying tuberous sclerosis, i.e., an expression of an "embryoplasmatic dysplasia."

SUMMARY

1. A case of tuberous sclerosis with associated pulmonary and skeletal changes has been presented.

2. The polycystic lung disease is considered to be an expression of "embryoplasmatic dysplasia."

3. The osseous manifestations may represent functional alterations due to neuroendocrine and neurovascular disorders, caused by the involvement of the hypothalamus and the vegetative nervous system.

REFERENCES

1. Barcroft, J. Features in the Architecture of Physiological Function. Cambridge University Press, 1938.
2. Berg, G., and Vejlens, G. Maladie kystique du poumon et sclérose tubéreuse du cerveau. *Acta paediat.*, 1939, *26*, 16–30.
3. Berg, G., and Zachrisson, C. G. Cystic lungs of rare origin—tuberous sclerosis. *Acta radiol.*, 1941, *22*, 425–436.
4. Bielschowsky, M., and Gallus. Ueber tuberöse Sklerose. *J. f. Psychol. u. Neurol.*, 1913, *20*, suppl., 1–88.
5. Bielschowsky, M. Zur Histopathologie und Pathogenese der tuberösen Sklerose. *J. f. Psychol. u. Neurol.*, 1923, *30*, 167–200.
6. Critchley, M., and Earl, C. J. C. Tuberose sclerosis and allied conditions. *Brain*, 1932, *55*, 311–346.
7. Freund, E. Osteodystrophia fibrosa unilateralis. *Arch. Surg.*, 1934, *28*, 849–866.
8. Gottlieb, J. S., and Lavine, G. R. Tuberous sclerosis with unusual lesions of the bones. *Arch. Neurol. & Psychiat.*, 1935, *33*, 379–388.
9.* Heublein, G. W., Pendergrass, E. P., and Widmann, B. P. Roentgenographic findings in the neurocutaneous syndromes. *Radiology*, 1940, *35*, 701–727.
10. Kveim, A. Ueber Adenoma sebaceum (Morbus Pringle), und seinen Platz im neurokutanen Syndrom—tuberöse Gehirnsklerose—und dessen Beziehung zur v. Recklinghausenschen Krankheit. Drei Fälle von tuberöser Sklerose und Morbus Pringle mit röntgenologisch nachweisbaren Veränderungen im Cerebrum und im Knochensystem, und Tumorbildungen in Retina. *Acta dermat.-venereol.*, 1937, *18*, 637–683.
11. Lichtwitz, Leopold. Functional Pathology. Grune & Stratton, Inc., New York, 1941.
12. Vejlens, G. Specific pulmonary alterations in tuberous sclerosis. *Acta path. & microbiol. Scandinav.*, 1941, *18*, 317–330.
13. Worster-Drought, C., Dickson, W. E. C., and McMenemey, W. H. Multiple meningeal and perineural tumours with analogous changes in the glia and ependyma (neurofibroblastomatosis), with report of two cases. *Brain*, 1937, *60*, 85–117.
14. Yakovlev, P. I., and Guthrie, R. H. Congenital ectodermoses (neurocutaneous syndromes) in epileptic patients. *Arch. Neurol. & Psychiat.*, 1931, *26*, 1145–1194.

* See for other references.

A NEW CHOLECYSTOGRAPHIC PREPARATION

By H. C. OCHSNER, M.D.*
INDIANAPOLIS, INDIANA

A RÉSUMÉ has been made of the results of 300 consecutive cholecystographic studies made during a period of three months, using a new contrast medium. The preparation, beta (4-hydroxy-3,5 diiodophenyl) alpha phenyl propionic acid, is supplied in tablet form and its administration is consequently simpler than that of tetraiodophenolphthalein. I have been particularly interested in the reactions experienced by patients who have taken this preparation and am firmly convinced that toxic reactions are less frequent and severe than with other contrast media; this without sacrifice of accuracy.

One hundred and sixty-nine, or 56 per cent, of the patients examined noted absolutely no untoward effects, and an additional 58 experienced slight reactions, making a total of 227, or 70 per cent, who had slight or no symptoms of toxicity. Reaction was moderate in 60, or 20 per cent, of the patients and severe in only 13, or 4 per cent.

Although nausea occurred in 70, or 26 per cent, of all cases, it was mild in 52, or two-thirds of this group. Nausea was associated with vomiting in only 8 patients, or less than 10 per cent of the group in which it occurred. In other instances, there was associated diarrhea, abdominal pain, pain on urination, or both. Diarrhea occurred in 46, or 15 per cent, of the total group; in most cases it was of slight or moderate severity. Abdominal pain was a complaint of 28, or 9 per cent, of the patients studied; it was severe in only 2 instances. Sixteen, or 5 per cent, of the patients complained of pain in the bladder area or pain on urination; this was slight in 5, moderate in 10, and severe in only one.

There was excellent, good or fair visualization in 201, or 67 per cent, of the total group and, of these, stones were demonstrated in 19, or 9 per cent. There was poor visualization in 93, or 31 per cent, of the total; stones were demonstrated in 39, or 42 per cent, of this number.

That intolerance to the medium was not the cause of the failure of satisfactory visualization of the gallbladder would appear to be proved by the fact that fewer reactions occurred in the poorly functioning or non-functioning group than in the group in which satisfactory visualization was obtained. Reactions were more severe in the patients who had demonstrable stones. In the normally functioning group without stones, 33 per cent of the patients had reactions of moderate or marked severity, while in the same group with stones, 47 per cent of the patients had reactions which were moderate or marked. In the non-functioning group without stones, only 7 per cent of the patients experienced moderate or severe reactions, while of this group in which stones were demonstrated, 23 per cent had similarly severe reactions.

Only 23 of these patients have been subjected to surgery but no error occurred which could be attributed to the method. In this series there has been no instance in which operation has been performed in a patient with "normally functioning gallbladder without stones." In 3 instances, in which diagnosis was made of "normally functioning gallbladder with stones," pathological findings were cholecystitis with stones. Two patients were explored who had "poorly functioning" gallbladders without demonstrable stones and in each chronic cholecystitis with stones was found. Diagnosis of "poorly functioning gallbladder with stones" was confirmed in 4 instances; evidence of cholecystitis was

* Radiologist, Methodist Hospital.

found, and stones were demonstrated. The accuracy of the diagnosis of "non-functioning" gallbladder was established in 14 patients. There was only 1 error and this cannot be attributed to the method. In the absence of a visualized gallbladder in this case, diagnosis of the presence of a small stone was incorrect but there was definite evidence of chronic cholecystitis. In 6 of the 7 patients who had "non-functioning" gallbladders in which stones were not demonstrated roentgenographically, stones were found by the surgeon. In each of 7 others with roentgenographically demonstrable stones, this finding was corroborated surgically.

SUMMARY

Priodax (Schering), beta (4-hydroxy-3,5-diiodophenyl) alpha phenyl propionic acid, a new preparation for cholecystography, has proved to offer many advantages over preparations previously in use. It is reliable, easy to take and produces fewer reactions than other cholecystographic media we have used. There is little or no residue of the medication in the bowel, because this substance is excreted largely through the kidneys, and this eliminates bowel shadows which are sometimes confusing. The gallbladder visualization which is produced is of ideal density to permit the demonstration of stones if they are present.

CHOLECYSTOGRAPHIC STUDIES WITH PRIODAX

By MAX DANNENBERG, M.D.
Roentgenologist, Beth-El Hospital
BROOKLYN, NEW YORK

THE discovery and development of cholecystography by Graham and his coworkers have been largely responsible for the great advances made in the study of the function and diseases of the gallbladder. Today the technique of roentgenologic examination of the gallbladder has been fairly well standardized.

The cholecystographic products on the market up to now have all been basically the sodium salt of tetraiodophenolphthalein under various trade names. It was first administered only by the intravenous route. However, because of the large number of severe reactions, Graham and his colleagues began to experiment with the oral method. Nausea and vomiting occurred to a lesser degree. If the patient vomited or a shadow of the gallbladder was not produced, the findings were confirmed both orally and intravenously. The oral method is the one of choice because of the convenience, both to the doctor and patient, the greater safety and the decreased number of reactions. The results approximate the accuracy of the intravenous method, as noted by Beilin and Carlson,[1] Kirklin,[3] and Robinson.[6]

Although the number of toxic reactions with sodium tetraiodophenolphthalein is considerably less by the oral method than by the intravenous, they occur often enough

FIG. 1. F.F. Good concentration of contrast medium within the gallbladder. Note absence of the medium in the colon.

FIG. 2. J.S. Good concentration within the gallbladder. Oblique view throwing the gas shadows away from the fundus.

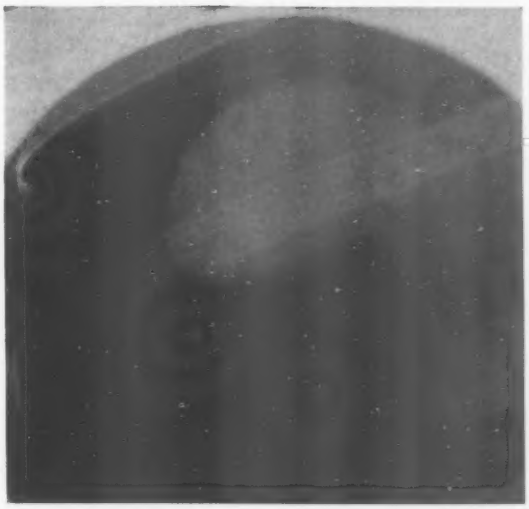


Fig. 3. D.T. Weight, 269 lb. Double dose of priodax. Good concentration within the gallbladder.

Fig. 5. Good concentration within the gallbladder. Note absence of contrast medium within the colon. Homogeneity of shadow.

to interfere with the efficacy of this drug. As we all know, the sodium salt of iodophenolphthalein is poorly tolerated by many patients. Severe reactions of vomiting, diarrhea and abdominal cramps are often experienced. Golden,[2] Levyn, Aaron,[4] and others, attempted to prevent gastrointestinal reactions by the use of fruit juices, alkalies and paregoric before the administration of the drug. The toxicity of the halogenated phenolphthaleins is due chiefly to the phenolphthalein part of the molecule. In addition to the toxicity, the laxative action of the phenolphthalein

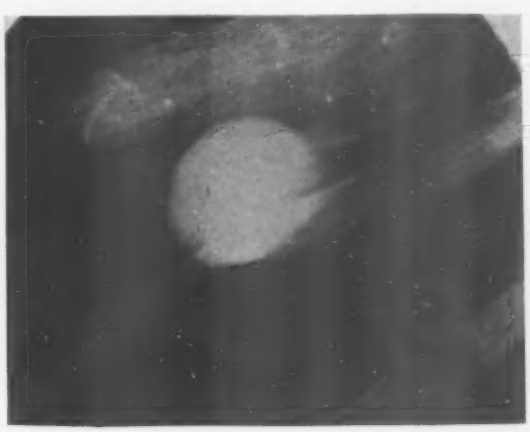


Fig. 4. Good concentration and normal visualization.

Fig. 6. Medium sized gallbladder. Absence of contrast medium in the colon aids in identifying the gallbladder.

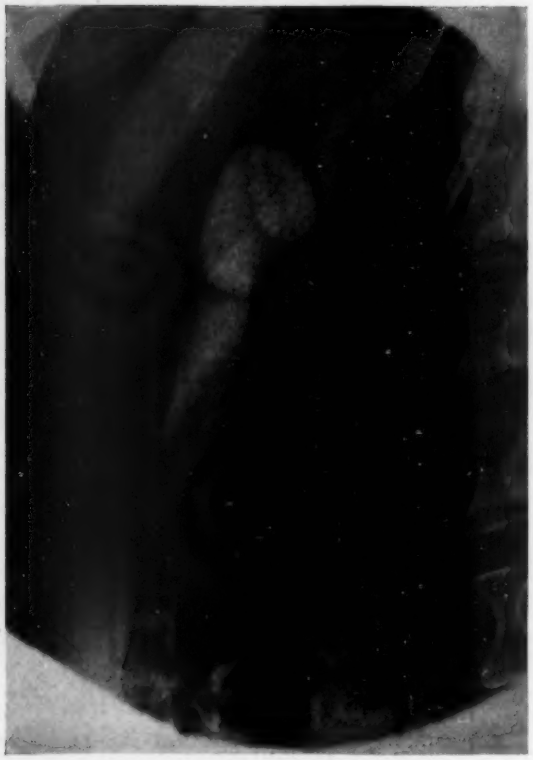


Fig. 7. Good concentration and even density of the gallbladder. There is a constriction in the mid-portion of the fundus. Operative findings: Pericholecystic adhesions with a kink in the middle of the fundus.

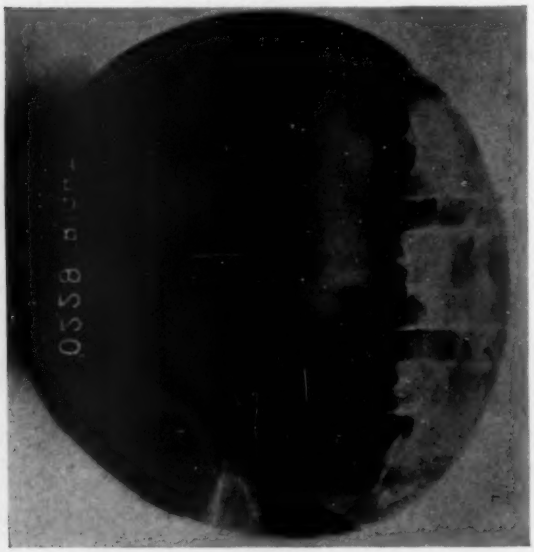


Fig. 8. Medium sized gallbladder of good concentration. There are numerous small, faceted, vacuolated areas which are characteristic of cholelithiasis.

Fig. 9. Fatty meal. The small, faceted, vacuolated areas are clearly visualized. There is a moderate evacuation of the contrast medium.

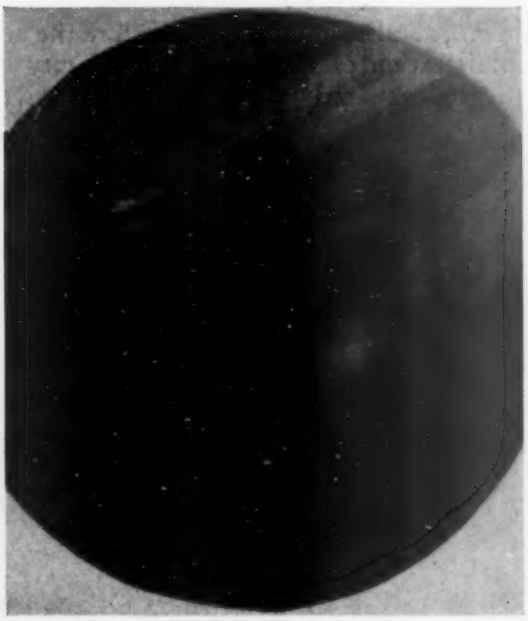


Fig. 10. Medium sized gallbladder of fair concentration. There are vacuolated areas in the region of fundus.

radical has added to the difficulties in the use of these preparations.

For the past year, I have administered a new drug with which these major objections have been largely overcome. This drug is beta-(3,5-diiodo-4-hydroxyphenyl) alpha phenol propionic acid, known under the trade name of priodax.* This new substance has no phenolphthalein radical in its composition and is totally unrelated to it. Priodax contains 52 per cent iodine, in firm combination, which absorbs roentgen rays strongly, but with no danger of dissociation, and therefore no possibility of iodism. It is a light, cream-colored powder and is practically tasteless. This new contrast medium is administered in tablets which may be swallowed or dissolved in water.

Priodax is easy to take and is well tolerated. With the elimination of the phenolphthalein radical, certain disadvantages of the old gallbladder dyes have been removed. One of the major advantages is the avoidance of any laxative action. The laxative effect of sodium tetraiodophenolphthalein is not only objectionable because of the inconvenience to the patient, but also because of the resultant decreased absorbability of the compound. Animal toxicity studies by Modell[5] showed no deleterious effects on the kidneys or liver. In addition to having no laxative action, priodax causes no severe gastrointestinal reactions. Vomiting rarely occurs, with the result that none of the drug is lost to lower its effectiveness.

In our series of 143 cases, there was 3 per cent of vomiting and negligible intestinal symptoms. It was evident that the absorption of the dye was satisfactory by the great percentage of good fillings and homogeneous shadows (Table 1).

There were no contrast-filled gas shadows obscuring the fundus of the gallbladder. The superimposed contrast-filled

* Made by the Schering Corporation.

FIG. 11. Oblique view of the same case as Figure 10 shows the vacuolated areas to be within the fundus and are characteristic of calculi.

FIG. 12. Numerous vacuolated, nucleated, calcified shadows within the fundus. Operative findings March 18, 1943, cholelithiasis and large stone in cystic duct.

Fig. 13. I.S. Weight, 200 lb. Double priodax. Oblique view shows medium sized gallbladder of good concentration. Vacuolated areas within the fundus which are characteristic of cholelithiasis.

intestinal shadows are seldom seen and the gallbladder can be easily identified.

The fact that priodax is taken orally eliminates many of the disadvantages of intravenous administration. For years, a drug has been sought which would be safe and at the same time effective when given by mouth. From my experience with priodax, it seems apparent that this new substance fulfills these requirements well. The use of a contrast medium intravenously has proved too toxic in many instances. Besides the toxicity, the possibility of producing thrombosis of the vein or necrosis of the perivascular tissues by accidental infiltration has always been a danger with intravenous administration. With priodax, we have a substance which is relatively free from side effects, conveniently and simply administered, and which produces excellent roentgenographic shadows.

TECHNIQUE

(1) The control roentgenogram is taken prior to the ingestion of the contrast medium.

(2) The patient is given a carbohydrate lunch.

(3) Six tablets (0.5 gm. priodax) are dissolved in one-fourth glass of water and one-fourth glass of fruit juice and then swallowed. The tablets may also be swallowed whole at ten minute intervals.

(4) No supper is taken.

(5) No breakfast is taken.

Table I

CHOLECYSTOGRAPHIC STUDIES WITH PRIODAX

Total cases	143		
Females	104		
Age 20–30	12		
31–40	33		
41–50	31		
51–60	14		
61–70	8		
Age not stated	6		
Males	39		
Age 10–20	2		
21–30	6		
31–40	11		
41–50	7		
51–60	12		
61–70	1		
Age not stated	0		
Method of Administration			
Swallowed whole	22		
Dissolved in water with fruit juice added	121		
Degree of Visualization			
Good	101		
Fair	11		
Poor or none	31		
Side Effects			
Nausea	24	7 slight	
Diarrhea	33	3 slight	
Vomiting	3		
Burning or pain on urination	24	13 slight	
males		14	
females		10	
Griping	29	13 slight	2 epigastric
Headache	2		
Burning in throat	6		
Belching	2		
Bitter taste	2		
"Greasy" taste	1		
Pain in back	1		
Severe reactions	0		
No reactions	9		

(6) The cholecystograms are taken fifteen hours after the oral ingestion and also after a fatty meal.

(7) If there are any gas shadows, an oblique view is always taken to throw the colon away from the fundus. This view is very valuable because gas shadows may be mistaken for calculi and also because small intrinsic calculi may be obscured by the colon. This is time saving and preferable to the use of the pressor agents, as advised by some.

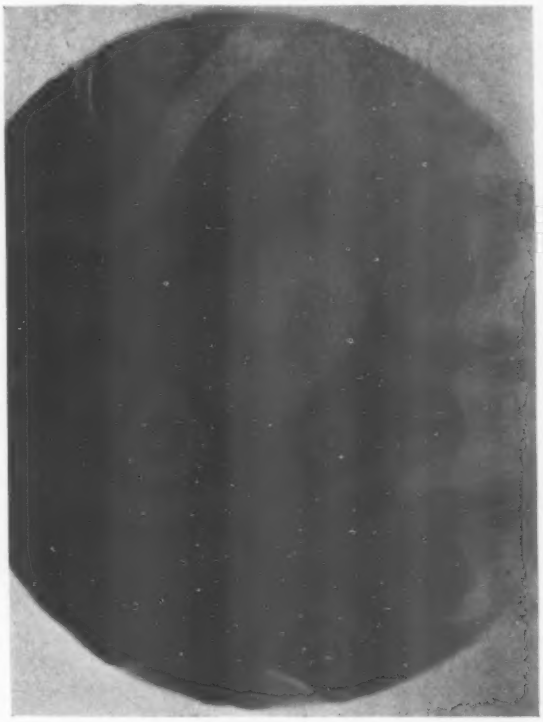


Fig. 14. Medium sized gallbladder of good concentration. Many vacuolated, faceted shadows within the fundus which are characteristic of cholelithiasis.

In our series the concentration of fair and good was over 85 per cent. The assurance of good concentration and certainty of identifying the gallbladder simplify the examination and conserve time. The clear, definite gallbladder shadows produced show the high rate of excretion through the liver. Optimal contrast density occurs in thirteen to fifteen hours. The clarity and distinctness of the gallbladder shadows with the use of priodax permit reliable diagnostic

Fig. 15. Medium sized gallbladder of good concentration. Numerous ovoid, faceted, vacuolated shadows within the fundus. A constriction in the proximal portion is probably ascribable to pericholecystic adhesions.

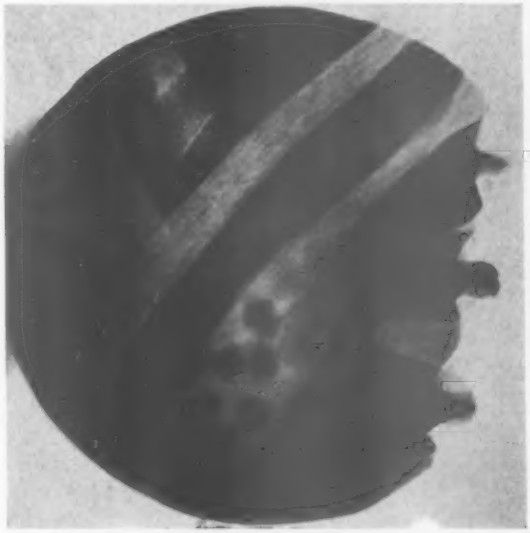


Fig. 16. Numerous sharply defined, vacuolated shadows within the fundus which are characteristic of cholelithiasis. Operative findings, September 16, 1942, confirm cholelithiasis.

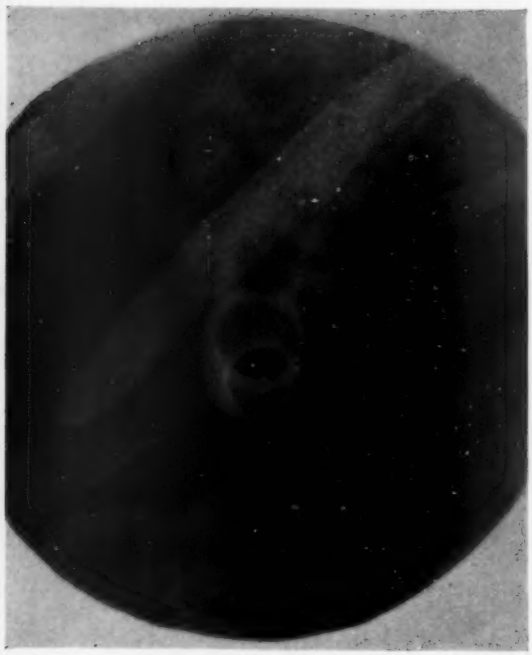


Fig. 18. Medium sized gallbladder with numerous vacuolated areas within the fundus which are characteristic of lithiasis.

Fig. 17. Medium sized gallbladder of good concentration. There are several vacuolated, ovoid areas filling the fundus. Gas in the colon is thrown away from the gallbladder shadows. Gas in the hepatic flexure is thrown away in this view clearing the fundus. Operative findings: November 27, 1942, cholelithiasis.

Fig. 19. Medium sized gallbladder with several well delineated, ovoid, vacuolated areas filling the fundus. Oblique view clears gas in the hepatic flexure away from the fundus.

differentiation between the visualized normal gallbladder and the non-visualized pathological gallbladder. At the same time, in cases of cholelithiasis, the shadows are light enough to permit good contrast with gallstones. This is of diagnostic value since too dense shadows may lead to errors by the masking of gallstones of the millet seed type.

SUMMARY

(1) The new contrast medium, priodax, is easy to take.

(2) There is a low incidence of vomiting, diarrhea and abdominal irritative reactions.

(3) There is a concentration of the contrast medium in a high percentage of cases.

(4) There are no obscuring contrast-filled intestinal shadows.

(5) No repeat examination is necessary.

(6) No alkalies, drugs, pressor agents or paregoric are necessary.

1464 Eastern Parkway
Brooklyn, New York

REFERENCES

1. Beilin, D. S., and Carlson, G. D. Clinical value of cholecystography by oral method. *Radiology*, 1931, *17*, 559–562.

2. Golden, Ross, Editor. Diagnostic Roentgenology. Renewal pages for Volumes I and II. Thos. Nelson & Sons, New York, 1941.

3. Kirklin, B. R. Necessity for accurate technique in oral cholecystography; errors attributable to technical lapses. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 595–601.

4. Levyn, L., and Aaron, A. H. Cholecystography by oral administration of sodium tetraiodophenolphthalein in solution. Am. J. Roentgenol. & Rad. Therapy, 1927, *18*, 557–559.

5. Modell, W. Pharmacology of β(3,5 di-iodo-4-hydroxyphenyl)α phenyl propionic acid. *J. Lab. & Clin. Med.*, 1942, *27*, 1376–1384.

6. Robinson, W. W. Oral cholecystography. *Radiology*, 1941, *36*, 131–144.

CALCIFICATIONS OF THE SPLEEN

By EDWIN F. GRAY, M.D.*
FLINT, MICHIGAN

CALCIFICATIONS of the spleen are occasionally encountered during roentgenographic examination of the abdomen or during necropsy. The literature contains numerous articles pertaining to this subject, and in view of the controversial nature of the reports of the etiology, this investigation was conducted in an effort to bring forth additional facts.

LITERATURE

The type of calcification most frequently reported is the small, multiple form, sometimes described as the miliary type. The first report was made by Mitchell[37] in 1919. Koppenstein[31] (1927) presented 8 case reports and maintained that they were due to calcified venous thrombi (phleboliths). However, he did not have microscopic proof in any of the cases. Courtin and Duken[12] reported 3 pediatric cases, thought to be of tuberculous origin, as there was demonstrable tuberculosis in other parts of the body. In one instance, they noted progressive calcium deposition in the spleen on a series of roentgenograms. Courtin and Duken stated that the cases reported by Koppenstein were similar to theirs and, as tuberculosis was present in other parts of the body, they should be considered tuberculous. Hellgren[23] observed the development of small calcified areas in the spleen of a child. Sweany[62] stated that 24.6 per cent of the patients who died of tuberculosis in the Chicago Municipal Tuberculosis Sanatorium had roentgenographic evidence of calcifications in the spleen. Sweany and Martinsen[60] reported 2 cases of calcified tuberculosis of the spleen confirmed by necropsy. In 1 case Spitz[56] based the diagnosis on the associated finding of renal tuberculosis and calcified pulmonary tuberculosis. Bársony and Schütz[3] reported phleboliths in 4 per cent of 180 spleens studied by roentgen examination and confirmed by microscopy. Berman[4] reported 18 cases, encountered during routine roentgenography of the abdomen. He considered the etiological factors of these cases to be: phleboliths, 11; questionable tuberculosis, 4; and doubtful 3. The 4 cases of questionable etiology were so considered because tuberculous lesions were found in other parts of the body. During routine roentgenography of 350 patients, Rudisill[47] discovered 4 instances of miliary splenic calcifications which he believed to be phleboliths, but offered no pathological proof. Henke and Lubarsch[24] discussed calcification of venous thrombi and presented as an illustration a case with many nodules. Moorman[39] reported 5 cases, 1 of which included necropsy findings. In 1 instance, fifty-six calcified nodules were found, while in another, there was associated calcification of the splenic artery. Dickson[13] reported 3 cases diagnosed as tuberculosis. In a pathological and roentgenological study of the evolution of calcified lesions (principally of the spleen) Sweany[58,63] conducted a study on a series of 20 tuberculous cases consisting of 16 adults and 4 children. Of these lesions, 16 had corresponding ages of lesions in the lungs, lymph nodes and spleen; 1 in the mesentery and spleen; 1 in the lungs, lymph nodes, liver and spleen; and in 2 there was no agreement of ages of the respective lesions. Bachman[1] reported 3 instances of calcified phleboliths but after further study[2] they were proved not to be phleboliths. Reichle and Work[46] encountered 71 spleens with calcified lesions during postmortem studies. Twenty guinea pigs were inoculated with material from the lesions in 14 cases. Positive "takes" were obtained in 4 animals from 3 of the cases.

* From the Departments of Radiology of the Presbyterian Hospital and of the College of Physicians and Surgeons, Columbia University, New York, New York.

Precautions had been taken to prevent contamination of the material, and no case was included if there was associated active miliary tuberculosis. Von Orelli,[41] Harrison,[20] Hektoen and Riesman,[22] Brown and Webb,[7] Camp,[11] Teschendorf,[64] and Ruhnau[48] also made reports on the miliary type of calcification. Wydler[68] in 1911 published the results of an extensive investigation, having demonstrated stones in ectatic vessels of the spleen. Jablons[28] reported a proved case in which marble-sized calculi were found in ectatic, hilar branches of the splenic vein. Möschl[38] reported 2 cases which on roentgenographic examination had multiple calcified areas. After reviewing the patients' history and the pathological findings, they were interpreted as inflammatory disease with secondary necrosis followed by calcium deposition. Meyer[36] reported a case having multiple calcified lesions as one of malarial thrombosis after finding concretions in the larger trabecular veins. Bignami and Secomandi[5] reported a case interpreted as being calcified pentastomiasis.

An entirely separate entity is that of the so-called primary tuberculosis which may be designated as such when that disease process may localize itself in the spleen and not only bring about various lesions, but act as a focus for dissemination of bacilli while the original focus may be healed entirely.[8]

Shands[53] and Bunch[8] reported instances of primary tuberculosis of the spleen with associated calcium deposition in which roentgenographic examination of the abdomen disclosed the presence of numerous calcified areas in the spleen. These nodules, however, were larger than in the foregoing type, measuring about 1 cm. in diameter. Three of the patients were treated by splenectomy and the diagnosis was confirmed. In 1 instance the nodule was reported to be due to an old bovine tuberculous infection.

Calcification of an aneurysm of the splenic artery is usually encountered on the roentgenogram as a circular area of calcium density in the region of the splenic artery. Heatley[21] observed 6 such cases. Tixier, *et al.*[65] reported a case in which two saccular aneurysmal dilatations of the splenic artery were present. Seids and Hauser[52] reported the case of a patient having a palpable mass associated with a 9 cm. calcified area medial to the spleen and interpreted as being a calcified aneurysm of the splenic artery. Israeleski,[27] Säfwenberg,[49] Sperling,[55] Högler,[25] and Lindboe[33] reported instances of calcified aneurysm which were proved at operation or necropsy.

Intracapsular hemorrhage with subsequent calcium deposition was reported by Mount, Mount and Hunter,[40] in which instance a female, aged forty-four, was found by roentgenographic examination to have a large area of calcium density in the splenic region. Her history pointed to an automobile accident three years previously, at which time moderately severe pain was present in the left upper quadrant of the abdomen. By ruling out other etiologic factors, they concluded that, at the time of the injury, intracapsular hemorrhage occurred and was followed by calcium deposition.

Calcified hemangioma or lymphangioma has been described by Ernst, Bowen, Ruggers, Wakeley, Hulten and Cowen. Ponzio[44] describes such a case, diagnosed because of its similar appearance to those previously described. Cole[11] reviewed the literature on cavernous hemangioma of the spleen, none of which were found to have calcified areas.

Calcification of the splenic capsule has been reported by Stott and Cotton-Cornwall[57] in which instance there was extensive calcification of the diaphragmatic surface. There was no evidence to indicate that the plaque was due to splenic inflammation or to direct spread from the thorax. Kröber[32] encountered another case, that of a fifty-five year old East African native who had generalized amyloidosis in addition to a draining sinus in the left upper quadrant of the abdomen. Operation disclosed a large spleen completely ensheathed in a bony capsule, broken in one place which was the origin of the tract. The etiological factor was not determined. Pallase, Santy and

Table I

Case	Age	Sex	Weight of Spleen (gm.)	Evidence of Systemic Tuberculosis	Roentgenogram of Spleen (Number of Lesions)
1*	44	M	100	None	12
2*	61	F	160	Healed tuberculosis of the peritoneum (miliary), lungs, mesenteric lymph nodes and spine. Caseous tuberculosis of adrenal	5
3*	65	M	120	Calcified tuberculosis of the liver	20
4	70	F	90	None	Calcification of splenic artery
5	60	F	70	None	2
6*	63	M	200	Calcified nodule in liver, possibly tuberculous	1
7	38	M	80	None	Calcification of splenic artery
8	45	F	220	None	5
9	60	M	210	Caseous pulmonary tuberculosis	6 Calcification of capsule
10*	58	F	285	Healed tuberculosis of hilar lymph nodes	8
11*	53	F	60	Healed apical tuberculosis	1
12*	49	F	140	Calcified tuberculosis of lung	3
13*	50	F	270	Healed apical tuberculosis	1
14*	35	F	260	Healed apical tuberculosis	1
15*	70	M	130	Apical scar	1
16*	2½	F	45	None	2
17*	53	M	280	Apical scar	3
18*	56	M	105	Calcified lesion of liver, possibly tuberculous. No apical scar	Calcification of capsule
19*	67	F	105	Apical scar	11
20*	54	F	260	Apical scar	2
21*	50	F	75	Healed tuberculosis of lung	1
22*	71	M	140	Adhesions of apical pleura	1
23*	50	F	220	Not examined	2
24*	58	F	85	Apical scar	Infarcts with calcification
25*	43	F	200	None	2
26*	21	F	170	No apical scar	2
27*	31	F	180	Tuberculosis of mesenteric lymph nodes	4
28*	37	M	250	None	1
29*	43	M	260	None	2
30*	54	M	200	Apical scar	2
31*	59	M	240	Tuberculosis of lung, spleen and hilar lymph nodes	4
32*	18	F	110	None	2
33*	58	M	340	None	Calcification of capsule
34*	63	F	710	Healed tuberculosis of lung, tuberculosis of tonsil	16
35*	45	F	140	Thickening of apical pleura	6
36*	41	M	440	Healed tuberculosis of lung	6
37*	73	M	200	Healed tuberculosis of lung	2
38*	80	M	260	Tuberculosis of lung, ileum	3

TABLE I—*Continued*

Case	Age	Sex	Weight of Spleen (gm.)	Evidence of Systemic Tuberculosis	Roentgenogram of Spleen (Number of Lesions)
					Calcification of splenic artery
39*	28	F	110	Lungs not examined	3
40*	41	M	170	Healed tuberculosis of lung	1
41*	80	M	60	Healed tuberculosis of lung	9
42*	59	F	110	Apical scar	1
43*	42	M	150	Healed tuberculosis of lung	6
44*	76	M	180	Thickening of apical pleura	8
45*	55	M	140	Healed tuberculosis of lung	5
46*	66	M	100	None	Calcification of capsule
47*	50	M	200	Healed tuberculosis of lung	2
48*	38	F	460	Apical scar	3
49*	48	M	250	None	1
50*	69	M	100	Healed tuberculosis of lung	4
51*	72	F	100	Apical adhesions	1
52*	66	M	280	Healed tuberculosis of lung	4
					Calcification of splenic artery
53*	55	M	180	Apical scar	2
54*	55	M	260	None	2
55*	33	M	220	None	4
56	50	F	150	Tuberculosis of the liver (miliary) and of the stomach, lung, gastric and hepatic lymph nodes	2
57*	72	M	300	Tuberculosis of spleen (miliary) and peritoneum	2
					Calcification of capsule
58*	57	M	320	None	3
59*	35	F	120	None	4
60*	50	M	240	Healed tuberculosis of lung and bronchial lymph nodes	60
61*	48	M	150	None	13
62*	71	F	170	None	4
63*	74	M	160	Tuberculosis of adrenal	12

* Examination included only one-half of the spleen.

Chanaleilles[42] reported an instance of painful perisplenitis with calcification, the symptoms of which were relieved by splenectomy.

Goinard[19] recorded the case of a male, aged fifty-seven, who had jaundice and splenomegaly. Four and one-half years after the onset of symptoms a roentgenogram of the abdomen dislosed calcified areas in the spleen, at which time there was eosinophilia and a positive intradermal reaction indicating the presence of a hydatid cyst. The diagnosis was confirmed by operation.

Three instances of calcium deposition in infarcts were recorded by Kadrnka and Babaiantz.[29] Their roentgenological diagnostic criteria are: (*a*) single or double intrasplenic calcareous foci having a triangular or oval form; (*b*) triangular shadows with apex toward the center and base toward the splenic capsule; (*c*) generally homogeneous calcification, either porous or soft, and (*d*) contours which are sharply

demarcated, but which may show small irregularities indicative of islands of absorption.

Calcified non-parasitic cysts of the spleen are quite rare. Fowler[17] reviewed the literature and mentioned cases reported by Kohnstamm, Piccinilli, Pean and Sphillman. Földes,[16] Gatersleven,[18] and Pool and Stillman[45] reported cases diagnosed roentgenologically. Calcification in the wall of a cyst has been reported by Scotson[51] in which instance a layer of calcium was found to measure $\frac{1}{32}$ inch in thickness. An instance is reported[66] in which roentgen studies disclosed a calcified mass the "size of an apple" in the splenic region which, after removal, was found to contain yellowish fluid and cholesterol plates. Shawan[54] reported an instance of an eighteen year old female who had a huge solitary cyst of the spleen with calcium deposits in its wall. Mattei[35] reported a case with multiple cysts having calcified walls. Bachman[1] presented a case of calcified cyst of the spleen, confirmed by necropsy.

Echinococcus cysts at times have calcium deposits in their walls in which case their roentgenographic appearance is that of a segmented or complete ring-like area of calcium density. Cases with roentgenograms have been reported by Boyd,[6] Downs,[14] Druckmann,[15] Holl,[26] and Calm.[9]

Kaufmann[30] stated that abscesses may calcify and that the *Pentastoma*, a parasitic anthropod, may form calcified nodules the size of a pea, which have been mistaken for phleboliths. Berman[4] cited such conditions as echinococcus cysts and bone forming metastases to be etiologic factors. Henke and Lubarsch[24] stated that trabecular calcification and bone formation occur and that calcium may be deposited in gummatous lesions.

MATERIAL AND METHODS

For this study, a group of 111 spleens from unselected necropsies have been subjected to roentgenographic examination. In most cases only one-half of the spleen was examined. Of this number, 63 (57 per cent) have evidence of calcification, from which the following classification has been made: multiple calcifications of the so-called miliary type, 58; calcification within the capsule, 5; calcification of the splenic artery, 5; and calcification within an infarct, 1. In some instances, lesions of more than one type have been found (Table 1).

Age Incidence. The ages range from two and a half to eighty years and may be classified by decades as follows: first decade, 1; third, 2; fourth, 8; fifth, 12; sixth, 19; seventh, 10; eighth, 8; and ninth, 2.

Sex Incidence. In this series the sex incidence is equal—31 male and 32 female.

Weights of Spleens. The relative occurrence of calcification according to the size of the organ is: 50–100 gm., 8; 100–200 gm., 26; 200–300 gm., 22; 300–400 gm., 3; 400–500 gm., 2; and 600–700 gm., 1.

Evidence of Systemic Tuberculosis. Eight cases have active systemic tuberculosis, while many others disclose evidence of apical scars of thickening of the apical pleura, which are possibly due to healed tuberculosis.

In 2 instances, there are calcified lesions in the liver which were interpreted by the pathologist to be calcified tubercles. Several instances of miliary tuberculosis are present.

Pulmonary infection is the most common site of systemic tuberculosis, while other sites of involvement are: hilar lymph nodes, mesenteric lymph nodes, adrenal, spleen, liver, stomach, ileum, peritoneum and vertebral column.

Multiple Calcifications. Roentgenographic examination shows the calcified areas to be distributed throughout the organ. In number, the lesions vary from one to sixty, but the majority of cases have less than ten. The diameter of the largest measures 8.25 mm. and that of the smallest is a fraction of 1 mm. In each case, one finds the size quite variable and not infrequently several lesions are present in a conglomerate mass. The most frequent configurations are ring like, oval or semilunar. Greater variation in shape is noted in specimens having the

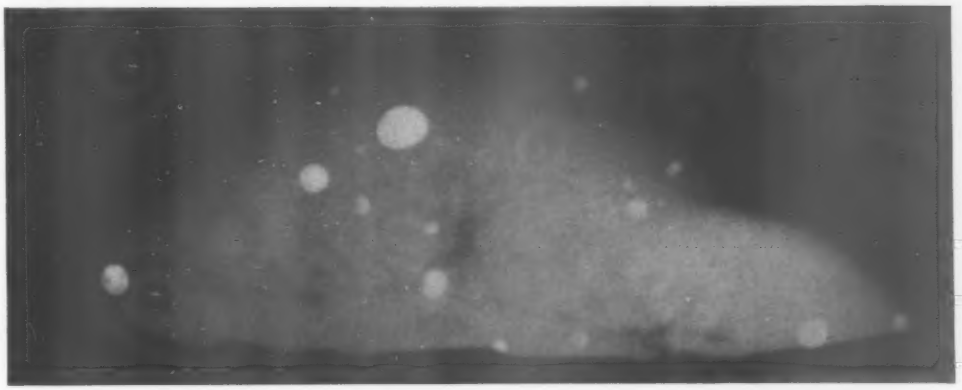


Fig. 1*A*. Roentgenogram of one-half of the spleen showing numerous calcified areas. Note the marked variation in size and shape of the lesions (see Case III).

largest number of calcium deposits (Fig. 1).

On gross examination, the lesions are found in all parts of the splenic pulp and in 1 instance a single nodule is found to be in a splenic fissure outside the capsule. The lesions vary in size from less than 1 mm. to almost 1 cm. The external appearance is that of a translucent, hyalinized mass which consists of a peripheral capsule and a central core. The diameter of the lesion is usually extremely large when compared to the size of the vessels of that vicinity. The capsule is soft and gelatinous and seldom contains calcium. Numerous trabecular and vascular attachments are present on the periphery but no occluded vessels are present. The capsule may be separated from the core and the consistency of the latter varies directly with the amount of calcium deposition. In the presence of little calcium, one finds the lesions to be gelatinous; however, with large amounts of calcium they are extremely hard. In the latter instance, the core frequently has a lamellated structure, consisting of yellowish glistening material which breaks with difficulty.

On microscopic examination, the peripheral portion of the lesion is actually a capsule of concentrically arranged hyalinized fibers. Interspersed with these fibers, one finds elastic tissue, either as loose fibers at the periphery or as one or two delicate layers which completely encircle the capsule. Occasionally the elastic tissue fibers form large masses. In no instance was there extensive calcification, although at times a water-marked appearance was noted as calcium deposits extended from the core. No smooth muscle fibers could be identified. The connective tissue fibers at times appear to be continuous with the trabeculae. No iron pigment is found. Occasionally one finds small areas of bone formation. In only one instance is there small round cell infiltration. Vessels from the trabeculae and pulp, when examined by serial sections, are frequently found to pass into the capsule, but no thrombosed vessels are associated with the calcified lesions. A distinct line of demarcation is usually seen between the capsule and core.

The center of the lesion may be considered as a core. The diameter of this core varies according to the size of the lesion, while the capsule maintains a somewhat uniform width in most instances. The diameter of the core is rather large in comparison with the width of the capsule. The shape varies in each instance, but the general contour is oval or round. The core may be divided into three types in accordance with the manner in which calcium deposition has taken place, as follows: (1) the entire lesion has a hyalinized appearance in which a small amount of calcium is deposited and one finds little to distinguish the core from the capsule; (2) the core is a large, more or less solid mass of calcium sur-

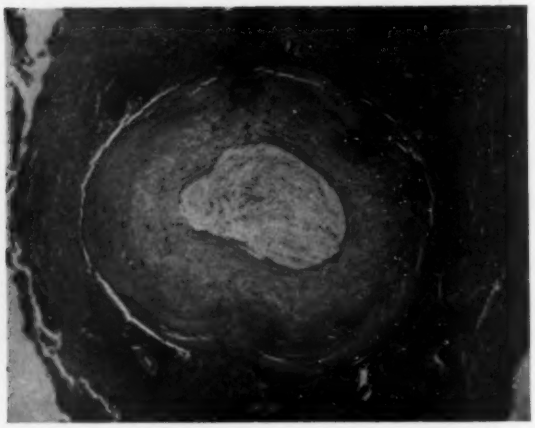


Fig. 1*B*. Photomicrograph (low power) of a single nodule in the spleen. The core contains many cholesterol clefts about which there are calcium deposits. There is no evidence of blood vessel wall or thrombus formation. The capsule has a hyalinized appearance.

rounded by a layer of loose connective tissue which separates the core and capsule; (3) the core is composed principally of loose connective tissue and cholesterol crystal clefts, the center of the core being essentially free of calcium, but peripherally one finds large calcium deposits which extend to and, at times, involve the capsule.

The types described above are not to be considered separate entities, as transitional

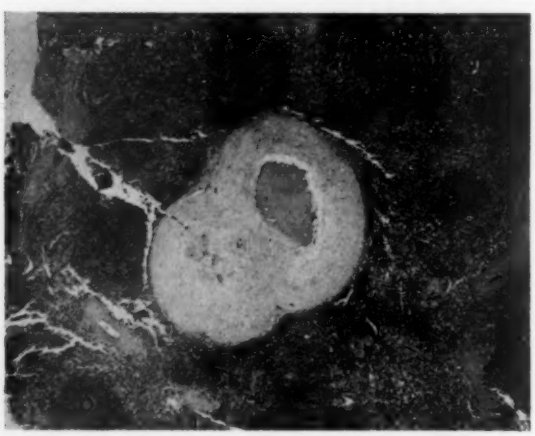


Fig. 1*C*. Photomicrograph (low power) of a double nodule in the spleen, the periphery of which contains numerous small round cells. The lesions have separate capsules which are attached in their periphery.

phases are noted. Occasionally one notes the presence of fibrin, polymorphonuclear leukocytes and lymphocytes, indicative of an inflammatory reaction. No tubercle bacilli were found. Hemosiderin is present in varying amounts, though elastic tissue fibers are not found. Serial sections frequently disclose bone formation, usually as multiple small areas. Bone marrow elements may be included. The calcium deposits appear either as granules or lamellated concretions, with the granular deposits being the most frequent type. The lamellated concretions varied considerably

Fig. 1*D*. Photomicrograph (× 110) showing a miliary tubercle immediately beyond the capsule of a calcified nodule.

in size and in no instance was this type found to the exclusion of calcium granules.

The splenic pulp about the lesions is not distorted to any great extent. As mentioned previously, the trabeculae are in close relationship to the capsule. In many instances there are unusually large amounts of hemosiderin about the lesion. Serial sections reveal no blood vessels that end within the wall of the calcified mass to indicate that thrombosis with occlusion of a vessel has taken place. Occasionally a vessel is distorted by the external pressure of a calcified area. The splenic veins are found to follow a rather straight course and in none is there tortuosity. Langhans' giant cells and tubercles are found in several cases, each of

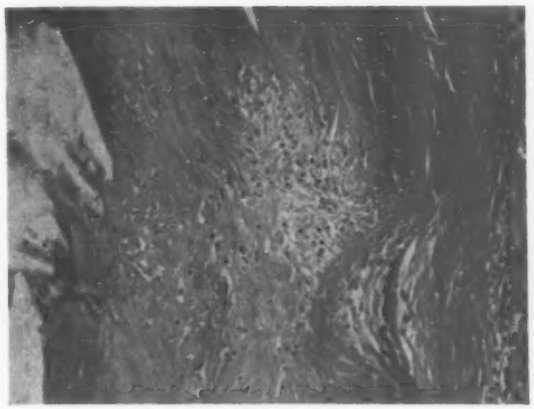


Fig. 1*E*. Photomicrograph (× 230) of a portion of a nodule with many cholesterol clefts and calcium concretions in the center. Numerous lymphocytes are present in the capsule. A thin layer of elastic tissue encircles a portion of the lesion.

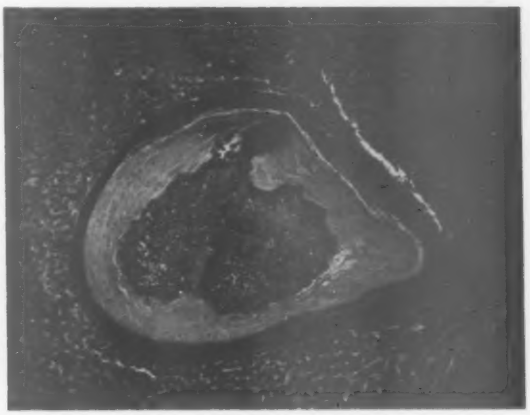


Fig. 1*G*. Photomicrograph (× 110) of a nodule in the liver, consisting of a core and capsule. Large calcium deposits are present in the center. This lesion has the same structure as those previously described in the spleen.

which has active tuberculosis in other organs.

In 2 instances guinea pigs were inoculated with a suspension of twenty-five and thirty fresh, crushed calcified nodules, respectively. At autopsy eight weeks later no tuberculosis was found.

Calcification within the Capsule. Roentgenograms disclosed 5 instances of calcium deposition within the capsule. The calcification is seen as a thin layer composed of granular deposits of calcium density distributed in a linear manner. In 1 case, the deposit included an area 0.5 by 15 cm., while in another it measured 2.5 by 3.5 cm. The areas were smaller in the 4 remaining cases.

Grossly, one finds the capsule to be free of adhesions, except in 1 instance in which there were dense fibrous adhesions to the diaphragm. In all cases there is thickening of the capsule and on section, one encounters calcium deposits. One case shows hyalinization with depression of a 2.5 by 3.5 cm. area of the capsule with calcium deposits limited to this region.

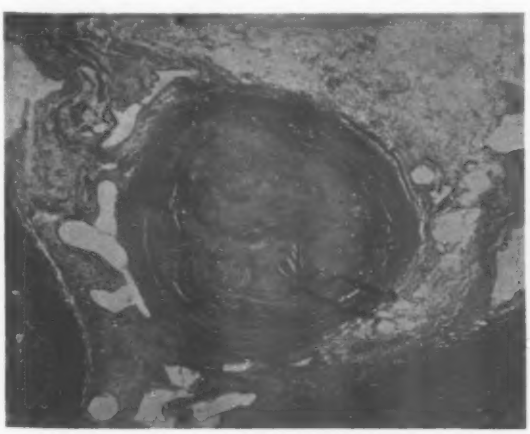


Fig. 1*F*. Photomicrograph (× 110) of a single nodule which lies entirely outside of the splenic capsule.

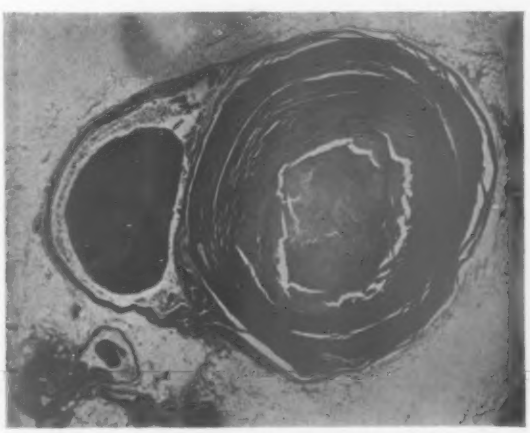


Fig. 1*H*. Photomicrograph (low power) of a cross section of a pelvic vein showing a calcified thrombus and vein wall. Large amounts of hemosiderin are present in the center.

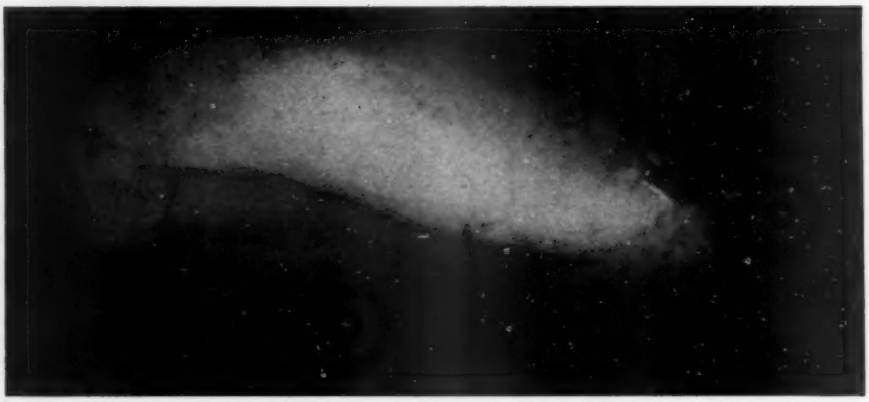


Fig. 2*A*. Roentgenogram of the spleen, showing mottled calcium deposits within the capsule.

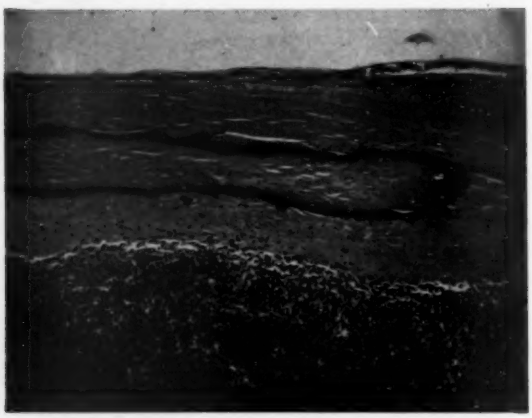


Fig. 2*B*. Photomicrograph (× 110) showing thickening and hyalinization of the splenic capsule in which there is a large calcium deposit. The adjacent splenic structure is normal.

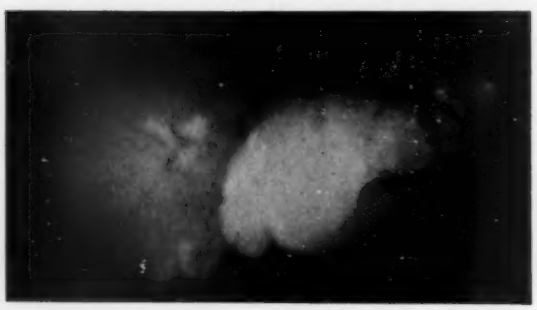


Fig. 3*A*. Roentgenogram of the spleen, showing mottled areas of calcium density having a triangular shape, the apex of which is directed toward the center of the organ.

Microscopic examination reveals considerable thickening of the capsule, the periphery of which is normal. In the deeper portion there is an unusually large amount of loose fibrous connective tissue. The tissue is relatively avascular and only a few small lymphocytes are present. Granular deposits of calcium are seen in this layer. No bone formation is noted (Fig. 2).

Calcification within an Infarct. In only 1 instance has there been calcium deposition within an infarct. The roentgenogram discloses four triangular areas in which there are deposits of calcium which have a granular appearance, the largest measuring 0.9

Fig. 3*B*. Photomicrograph (× 40) showing extensive fibrosis about an occluded artery. Numerous calcium deposits and large amounts of hemosiderin are present.

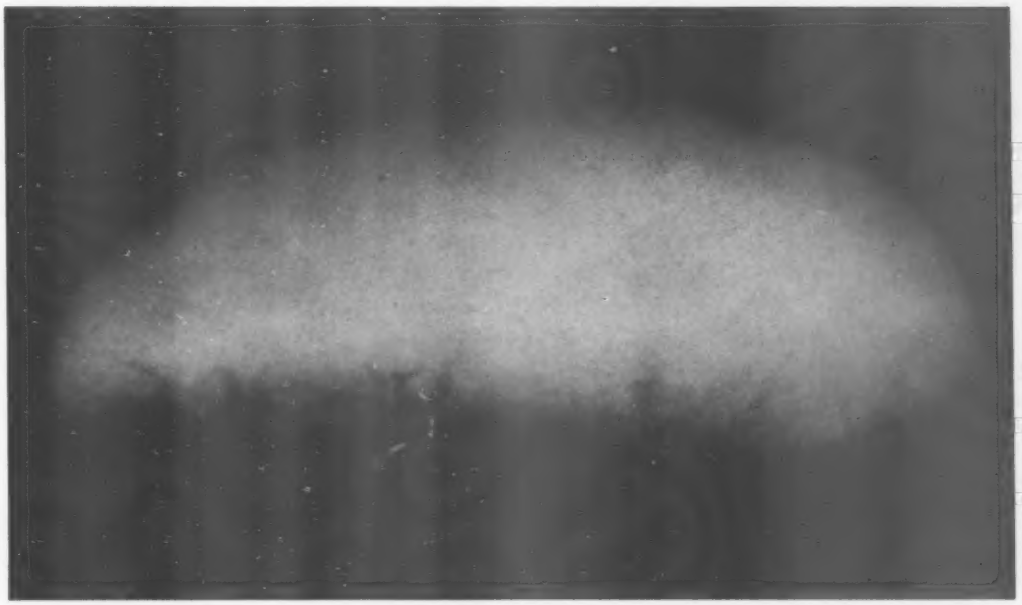


Fig. 4*A*. Roentgenogram of a portion of the spleen, showing calcium plaques within the splenic artery in the region of the hilum.

by 1.8 cm. In each instance the apex is directed toward the center and the base toward the periphery of the spleen (Fig. 3).

The external appearance of the spleen is normal. However, on sectioning, one encounters triangular areas of increased resistance in which calcium deposits are present. The cut surface is slightly darker than the surrounding tissue and has a mottled appearance.

Microscopic examination shows the capsule to be slightly thicker than normal. Immediately beneath the capsule, one sees a sharply demarcated area in which the splenic pulp is replaced by moderately dense fibrous tissue. A small number of small round cells are present, as well as numerous capillaries and small blood vessels. There is a large amount of yellowish-brown refractive pigment. Near the inner margin of the lesion one finds several occluded blood vessels. Diffuse granular deposits of calcium are noted, but there is no evidence of cancellous bone formation.

Calcification of the Splenic Artery. The roentgenographic findings are the same as those of calcification in other vessels, i.e., circular or mottled shadows of calcium density in the course of the splenic artery. These deposits may occur in the splenic artery or in its branches within the splenic pulp (Fig. 4). The calcification may involve only a few millimeters or the entire length of the vessel. However, in this group all calcifications are in the hilum or in vessels

Fig. 4*B*. Photomicrograph (low power) of a section of the splenic artery, showing a large area of intimal thickening in which calcium deposition has occurred. The lumen is considerably narrowed.

within the splenic pulp, but near the hilum.

On gross examination the diameter of the vessel is found to be relatively small when compared to the normal. Microscopic examination discloses marked intimal thickening in the form of a large plaque that is composed chiefly of collagen. In the deeper part, this has undergone degeneration; calcium and cholesterol clefts are found in the degenerated area. In one part there is slight mononuclear cell infiltration in the plaque. There is a loss of nuclei in the media and a deposition of calcium in fine granules. The adventitia is normal.

DISCUSSION

It has been demonstrated conclusively that splenic calcifications of the so-called miliary type occur irrespective of the age or sex of the patient. The number of the calcified lesions varies from one to sixty; however, the majority of cases contain less than a dozen. Actually the nodules are more numerous as only one-half of the organ was subjected to examination in most instances. The roentgenographic characteristics of the lesions are explained by the manner in which calcium deposition occurs. Necropsy disclosed evidence of systemic tuberculosis in a small portion of the cases. However, the majority of the cases were found to have apical scars and thickening of the apical pleura, which are possibly the result of healed tuberculosis.

A single extracapsular lesion was found to contain questionable epithelioid cells and Langhans' giant cells, but no evidence of thrombus formation. In such an instance it seems probable that this lesion is a healed tubercle rather than a phlebolith.

Gross and microdissection, as well as microscopic serial sections, were made on these lesions. Similar studies were made on calcified venous thrombi in the pelvic vessels in order to have a control. In no instance is there direct evidence to indicate that the etiology of the splenic calcifications is either tuberculosis or thrombosis. In addition, no occluded veins are present in the adjacent pulp. The diameter of calcified lesions in the spleen is always much greater than that of the veins in that region. The splenic veins are not tortuous. In comparison, the pelvic veins are markedly tortuous and the diameter of the phlebolith is rarely more than twice as large as that of the diameter of the associated vein. The multiplicity of the lesions is one point in favor of miliary tuberculosis as the etiologic factor. Disseminated tuberculosis frequently involves all portions of the organ but it seems unlikely that thrombi would occur in such a manner. In the event that a splenic thrombus should calcify, it would most likely be associated with residual fibrosis and such was not found here. Bone formation, including bone marrow elements, is present in the splenic lesions, as well as in the pelvic phleboliths.

Hemosiderin is frequently present in small amounts but not in such a manner as to indicate the presence of a thrombus.

Considerable elastic tissue is present in the wall of the lesions. In a few instances the fibers encircle the lesions. However, they do not have the appearance of the elastic tissue fibers which are found in blood vessels. Neither can the associated hyalinized fibers be identified as a blood vessel wall.

Of all the organs of the body the spleen has the maximum phagocytic capacity for tubercle bacilli.[34,43] Knowing that a large percentage of the cases were found at necropsy to have evidence of systemic tuberculosis, it is quite possible that miliary tuberculosis of the spleen was present at some period during the life of the patient.[67] As the most retrogressive process in the course of tuberculosis (Sweany,[59] and Sweany, Tillotson and Kozielek,[61]) one would frequently expect healed tuberculosis of the spleen. The presence of similar lesions in the liver is evidence favoring tuberculosis as the etiologic factor.

Guinea pig inoculation was performed in 2 cases and after eight weeks there was no evidence of tuberculosis. The inability to find acid-fast bacilli in only 2 cases cannot be regarded as conclusive. Reichle and

Work[46] obtained positive "takes" in 4 animals of 3 cases.

Each of the 5 instances of calcium deposition within the capsule is associated with hyalinization which occurs as a degenerative change. In 1 instance there were adhesions between the spleen and the diaphragm, but as the calcium deposits are identical to those in which adhesions are absent, it is improbable that perisplenitis is the etiologic factor. This type of lesion is present only in patients of an advanced age.

The only case of calcium within an infarct is recognized by its gross, microscopic and roentgenographic characteristics.

Four cases of calcification of the splenic artery have been encountered. The calcium deposits represent an advanced stage of arteriosclerosis and involve small areas in most instances. Aneurysmal changes have not been encountered. With the exception of 1 patient, aged thirty, all patients were of an advanced age. Other instances of calcifications of the spleen encountered during routine roentgenographic examination of the abdomen are: multiple calcifications, 50; calcification of the splenic artery, 2; and calcification in an aneurysmal dilatation of the splenic artery, 1 (Fig. 5).

Several illustrative case reports follow.

Case 1 (Unit No. 501768). A white female, aged sixty-three, was admitted April 18, 1938, because of repeated attacks of epigastric pain and jaundice of five years' duration. Nausea and vomiting accompanied the pain. Physical examination was negative.

Roentgenographic examination of the abdomen disclosed the presence of gallbladder calculi. The spleen was normal in size. In the region of the splenic artery there were several sharply demarcated, ring-like shadows of calcium density, the largest of which measured 1.5 by 2.5 cm. A diagnosis of aneurysmal dilatation of the splenic artery was made (Fig. 5).

Cholecystectomy was performed on April 27, 1938. At the time of operation, the splenic artery was found to be firm, tortuous and dilated, with evidence of calcification. These findings confirmed the roentgenological interpretation.

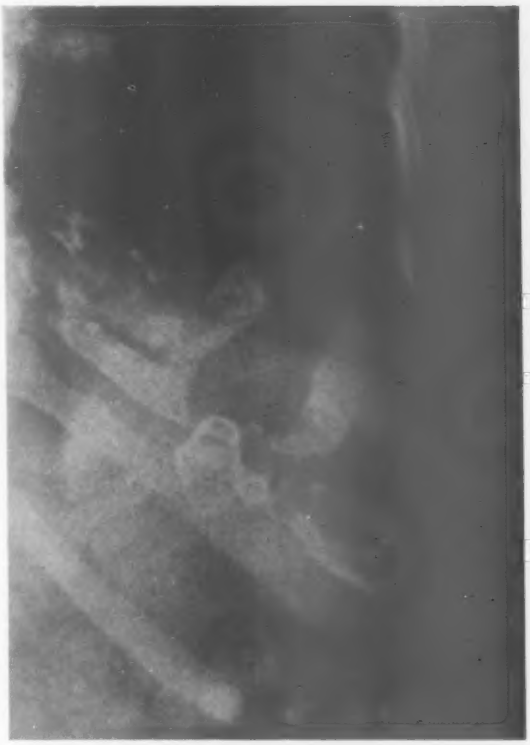


Fig. 5. Case 1. Roentgenogram of the abdomen showing the ring-like shadows in the region of the splenic artery at the hilum. At operation this was found to be a calcified aneurysmal dilatation of the splenic artery.

Comment. A calcified aneurysmal dilatation of the splenic artery was diagnosed by roentgenographic examination and confirmed at operation. No symptoms could be attributed to this lesion.

Case 11 (Unit No. 315675). A white female infant, aged eight months, was admitted October 5, 1931, with a history of pneumonia two months previously, after which the infant failed to gain weight. The illness accompanying the pneumonia persisted for about three weeks. At the time of the acute illness, the patient weighed 15 pounds, while at the time of admission she weighed only 10 pounds. Three days before admission, she suddenly began to refuse all food.

Physical examination showed the patient to be dyspneic, markedly dehydrated and undernourished. The temperature was elevated to 101°F. Evidence of acute otitis media, left, was present. Large, firm lymph nodes were

Fig. 6. Case II. Roentgenogram showing calcified areas in the spleen, liver and lymph nodes (mesenteric, inguinal and prevertebral). Disseminated pulmonary tuberculosis is present.

palpable in the cervical and occipital regions. There were questionable signs of pneumonia in the left lower lobe.

Roentgenographic examination disclosed the presence of miliary tuberculosis of the lungs. In the region of the spleen and liver there were many small oval shadows of calcium density, predominantly in the former (Fig. 6). In addition, there were shadows in the mesenteric, cervical, inguinal and prevertebral lymph nodes, suggestive of calcium deposits within tuberculous lesions.

Following admission, the temperature was persistently elevated. The râles persisted and signs of cavitation developed in the right apex. Incision and drainage of a cervical lymph node liberated a large amount of greenish pus, in which tubercle bacilli were demonstrated. The patient became more acutely ill and the temperature rose to 105°F. Death occurred thirteen days following admission. Necropsy was not permitted.

Comment. This case is one of acute miliary tuberculosis, complicated by tuberculous otitis media and mastoiditis. Calcium deposits were in the lymph nodes, liver and spleen, demonstrated by roentgen examination, all of which undoubtedly represent calcium deposition with tubercles.

Case III (Unit No. 456835). A white female, aged sixty-one, was admitted January 30, 1936, because of pain in the lumbar spine. A diagnosis of Addison's disease had been made four years previously. Pott's disease had been present for several years and was accompanied by a pain referred to the anterior aspect of the thighs. Mechanical appliances to her spine relieved the pain temporarily.

Physical examination showed the patient to be quite emaciated. A generalized pigmentation of the skin was present. There was a kyphosis at the level of the third and fourth lumbar vertebrae, without associated tenderness.

Roentgenographic examination of the chest disclosed evidence of tuberculosis of the left upper lung associated with calcium deposition. There was destruction in the third and fourth lumbar vertebrae and the adjacent intervertebral disc, resulting in a kyphosis. Examination of the abdomen revealed calcium deposits in the mesenteric lymph nodes (Fig. 7) and spleen.

Course. Three days after admission, the patient became comatose. The blood sugar at that time was 45.2 mg. per 100 cc. She returned to consciousness after the intravenous administration of cane sugar. One day later the blood pressure fell to 82/46 from 140/80 and her temperature became elevated. Physical examination disclosed no cause for the persistent fever, though diminished breath sounds were noted in the right lower chest posteriorly. The blood pressure remained lower than normal and death occurred February 10, 1936.

Necropsy disclosed the presence of healed tuberculosis of the lungs, retroperitoneal lymph nodes and peritoneum (miliary). A kyphosis was present in the lumbar region due to destruction of the third and fourth lumbar vertebrae. Fibrocaseous tuberculosis of the adrenals was present. Numerous calcified areas were present in the spleen.

SUMMARY

1. The literature on calcifications of the spleen is reviewed.

Fig. 7. Case III. Roentgenogram of the abdomen, showing calcified areas in the spleen and mesenteric lymph nodes. Tuberculosis of the third and fourth lumbar vertebrae is associated with destruction of the intervertebral disc and partial collapse of the vertebral bodies. The shadows indicated by arrows are intestinal artefacts.

2. Calcifications of the spleen are frequently encountered during roentgenographic examination of the spleen and at necropsy. Sixty-three cases are reported, an incidence of 57 per cent.

3. The most frequent types of lesions are: miliary calcified lesions, calcification of the splenic artery, calcification of the splenic capsule and calcium deposition within healed infarcts.

4. Miliary calcification may occur at any age, but most commonly after thirty years of age. Calcifications of infarcts, the capsule and splenic artery usually occur in patients of advanced age.

5. The so-called miliary calcifications apparently represent calcified miliary tubercles.

6. Evidence of systemic tuberculosis, active or inactive, is present in most instances.

7. The roentgenologic and pathologic features of the various types of splenic calcifications are discussed.

8. Other instances diagnosed by roentgenographic examination during life are mentioned.

REFERENCES

1. Bachman, A. L. Calcifications in splenic region. Am. J. Roentgenol. & Rad. Therapy, 1931, *41*, 931–949.
2. Bachman, A. L. Calcifications in the splenic region. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 607–608.
3. Bársony, T., and Schütz, O. Phlebolithen in der Milz. *Röntgenpraxis*, 1931, *3*, 68–73.
4. Berman, T. M. Miliary calcifications in the spleen. *Radiology*, 1937, *29*, 37–39.
5. Bignami, G., and Secomandi, G. M. Parassiti epatici e splenici (Pentastomi in particolare) al controllo radiologico ed anatomo-istologico. *Arch. di radiol.*, 1939, *15*, 227–254.
6. Boyd, D. Echinococcus cyst of spleen. *Boston M. & S. J.*, 1925, *193*, 591–593.
7. Brown, L., and Webb, G. B. Discussion of paper by Shands.[53]
8. Bunch, G. Primary tuberculosis of spleen, with report of case simulating Banti's disease. *South. M. J.*, 1931, *24*, 764–768.
9. Calm, A. Demonstration seltener Röntgenbefunde; (d) Echinokokkus der Milz. *Verhandl. d. deutsch. Röntg.-Gesellsch.*, 1921, *12*, 135–136.
10. Camp, J. D. Discussion of paper by Shands.[53]
11. Cole, F. L. Personal communication.

12. Courtin, W., and Duken, J. Ueber Milztuberkulose und ihre röntgenologische Darstellbarkeit. Zugleich ein Beitrag zur Kenntnis der hämatogenen Tuberkuloseausbreitung im Kindesalter. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1928, *37*, 836–839.
13. Dickson, W. H. Diagnosis of obscure abdominal lesions by roentgen gastrointestinal examination. Am. J. Roentgenol. & Rad. Therapy, 1923, *10*, 540–546.
14. Downs, T. McK. Parasitic cysts of the spleen. *Proc. Path. Soc. Philadelphia*, 1925, *27*, 29–30.
15. Druckmann, A. Die Röntgendiagnose des verkalkten Echinokokkus. *Forschr. a. d. Geb. d. Röntgenstrahlen*, 1928, *37*, 697–700.
16. Földes, A. Milzcyste mit verkalkte Wand. *Zentralbl. f. d. ges. Radiol.*, 1927, *3*, 346.
17. Fowler, R. H. Cystic tumors of the spleen. *Internat. Abstr. Surg.*, 1940, *70*, 213–223.
18. Gatersleben, H. Ein Beitrag zu den Milzzysten. *Deutsche Ztschr. f. Chir.*, 1928, *212*, 139–149.
19. Goinard, P. Calcified hydatid cyst of the spleen. *Bull. et mém. Soc. nat. de chir.*, 1934, *60*, 1360–1362.
20. Harrison, B. J. M. Textbook of Roentgenology, William Wood & Co., Baltimore, 1936, pp. 179–183.
21. Heatley, J. E. Calcification of splenic artery. *Radiology*, 1935, *24*, 235.
22. Hektoen, L., and Riesman, D. An American Textbook of Pathology. W. B. Saunders Co., Philadelphia, 1902, p. 553.
23. Hellgren, E. G. Fall von Miliartuberkulose im Kindesalter, der—mit röntgenologischen Residuen u. a. in der Milz—zu klinischer Heilung kam. *Acta paediat.*, 1932, 180–194.
24. Henke, F., and Lubarsch, O. Handbuch der speziellen pathologischen Anatomie und Histologie. J. Springer, Berlin, 1931.
25. Högler, F. Beitrag zur Klinik des Leber- und Milzarterienaneurysmas. (Zugleich im Beitrag zur systematischen Auskultation der Bauchgefässe.) *Wien. Arch. f. inn. med.*, 1920, *1*, 509–562.
26. Holl, E. Ein Fall von Echinokokkuserkrankung der Milz. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1928, *37*, 862–863.
27. Israelski, M. Die verkalkte Arteria lienalis im Röntgenbilde. *Röntgenpraxis*, 1930, *2*, 670–672.
28. Jablons, B. Concretions of the spleen. *California State M. J.*, 1916, *14*, 103–105.
29. Kadrnka, S., and Babaiantz, L. Etude radiologique de l'infarctus de la rate; diagnostic différentiel der calcifications spleniques. *J. de radiol. et d'électrol.*, 1934, *18*, 161–169. Abs. Year Book of Radiology, Year Book Publishing Co., Chicago, 1934, p. 131.
30. Kaufmann, E., and Reimann, S. P. Pathology. P. Blakiston's Son & Co., Philadelphia, 1929.
31. Koppenstein, E. Phlebolithen in der Milz. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1927, *36*, 139–144.
32. Kröber, F. Ein seltener Fall von Perisplenitis ossificans. *München. med. Wchnschr.*, 1936, *83*, 179.
33. Lindboe, E. F. Aneurysm of splenic artery diagnosed by x-rays and operated upon with success. *Acta chir. Scandinav.*, 1932, *72*, 108–114.
34. Lurie, M. B. Fate of human and bovine tubercle bacilli in various organs of the rabbit. *J. Exper. Med.*, 1928, *48*, 155–182.
35. Mattei. Cited by Fowler.[17]
36. Meyer, Richard. Stone formation in spleen after malaria as a cause of sickness. *Wien. klin. Wchnschr.*, 1936, *49*, 1496–1498.
37. Mitchell, W. Splenic calculi. *Arch. Radiol. & Electrol.*, 1919, *24*, 59–60. Abs. Am. J. Roentgenol., 1920, *7*, 123.
38. Möschl, H. Kalksteine in Milzen. *Virchow's Arch. f. path. Anat.*, 1936, *298*, 37–43.
39. Moorman, L. J. Multiple calcifications in the spleen. *Am. Rev. Tuberc.*, 1937, *36*, 376–386.
40. Mount, G., Mount, F. R., and Hunter, W. C. Calcification in the spleen. *J. Am. M. Ass.*, 1936, *107*, 203–205.
41. von Orelli, A. Ueber verkalkende Tuberkulose der Milz. *Arch. f. klin. Med.*, 1938, *183*, 264–276.
42. Pallase, Santy, P., and Chanaleilles. Cited by Bachman.[1]
43. Perla, David, and Marmorston, Jessie. The Spleen and Resistance. Williams and Wilkins Co., Baltimore, 1935.
44. Ponzio, M. Multiple calcified angiomas in liver and spleen. *J. belge radiol.*, 1932, *20*, 218.
45. Pool, E. H., and Stillman, R. G. Surgery of the Spleen. D. Appleton & Co., New York, 1923.
46. Reichle, H. S., and Work, J. L. Incidence and significance of healed miliary tubercles in the liver, spleen and kidneys. *Arch. Path.*, 1939, *28*, 331–339.
47. Rudisill, H., Jr. Calcifications in the spleen. Am. J. Roentgenol. & Rad. Therapy, 1932, *28*, 805–807.
48. Ruhnau, A. Ein Fall von tuberkulösen Kalkherden in der Milz. *Tuberkulose*, 1933, *13*, 172–173.
49. Säfwenberg, O. Zwei röntgenologisch Diagnostizierte Falle von Milzarterienaneurysma. *Acta radiol.*, 1937, *18*, 481–490.
50. Schottenfeld, L. E., and Wolfson, W. L. Cavernous hemangioma of the spleen. *Arch. Surg.*, 1937, *35*, 867–877.
51. Scotson, F. H. Calcified cyst of spleen. *Brit. M. J.*, 1933, *1*, 367.
52. Seids, J. V., and Hauser, H. Cited by Sperling.[55]

53. Shands, H. R. Chronic primary tuberculosis of spleen, x-ray diagnosis. *Am. J. Surg.*, 1933, *20*, 707–721.
54. Shawan, H. K. Calcified cyst of spleen. *Ann. Surg.*, 1937, *106*, 469–474.
55. Sperling, L. Aneurysm of splenic artery. *Surgery*, 1940, 8, 633–638.
56. Spitz, L. Zur Frage der Venensteine und der tuberkulösen Kalkherde in der Milz. *Röntgenpraxis*, 1932, *4*, 993–997. Abs. in Year Book of Radiology, Year Book Publishing Co., Chicago, 1933, p. 378.
57. Stott, L. B., and Cotton-Cornwall, V. Case of pathological calcification. *Lancet*, 1933, *2*, 755–757.
58. Sweany, H. C. Studies on pathogenesis of primary tuberculous infection; regressive lesions. *Am. Rev. Tuberc.*, 1933, *27*, 559–574.
59. Sweany, H. C. Personal communication.
60. Sweany, H. C., and Martinsen, W. L. M. Incidence of extrapulmonary primary tuberculosis. *Am. Rev. Tuberc.*, 1938, *37*, 465–483.
61. Sweany, H. C., Tillotson, A. E., and Kozielek, V. Studies on retrogressive changes of tubercles. *Am. Rev. Tuberc.*, 1938, *37*, 484–493.
62. Sweany, H. C. Cited by Moorman.[39]
63. Sweany, H. C. On the nature of calcified lesions; with special reference to those in the spleen. Am. J. Roentgenol. & Rad. Therapy, 1940, *44*, 209–229.
64. Teschendorf, W. Die Röntgendiagnostik von Leber, Milz und Pancreas. *Jahrb. f. Röntgenol.* Walter de Gruyter & Co., 1931, p. 116. Cited by Bachman.[1]
65. Tixier, Baumgartner, Ronneaux, and Gadreau. Anévrismes calcifiés de l'artère splénique et splénomegalie. *Bull. et mém. Soc. de radiol. méd. de France*, 1930, *18*, 349–351.
66. Waters, C. A., and Kaplan, I. I., Editors. Year Book of Radiology, Year Book Publishing Co., Chicago, 1936, p. 378.
67. Winternitz, M. C. Tuberculosis of spleen. *Arch. Int. Med.*, 1912, *9*, 680–697.
68. Wydler, A. Cited by Bachman.[1]

CONGENITAL ABSENCE OF THE PATELLAE ASSOCIATED WITH ARTHRODYSPLASIA OF THE ELBOWS AND DYSTROPHY OF THE NAILS

A HEREDITARY SYNDROME*

By HYMAN R. SENTURIA, A.B., M.D.† *and* BEN D. SENTURIA, B.S., M.D.
ST. LOUIS, MISSOURI

SINCE the last part of the nineteenth century there have appeared in the literature, from time to time, isolated reports dealing with the unusual association of malformations of the nails, hypoplasia or complete absence of the patellae, and deformities with impaired function of the elbows. In many cases this triad has been inherited, in varying modifications, in several generations of the same family, while in others, one or more of the cardinal features have been absent or altered. This condition is purely inherited and congenital and is apparently due to some developmental defect in the ectodermal and mesodermal layers of the embryo. In 1897 Little[7] reported 42 cases of congenital absence or delayed development of the patella, collected from the literature, to which he added 3 cases of his own. In his article he mentions a family observed by Sedgwick in four generations of which 18 persons had no patellae and no thumb nails. The majority of these cases were females, but there is no mention as to whether every member was affected or whether the two deformities were always associated. Wolf[23] in 1900 reported a family in which the mother showed congenital absence of both patellae and complete absence of both thumb nails. Her two children, a son and a daughter, inherited the same deformities, while her grandchildren were perfectly normal. In 1903 Most[9] called attention to a family in which absence of the thumb nail and extensive atrophy of the remaining nails of the mother were inherited by all 6 sons. One of the 6 is the father of the child under observation. The patient had, in addition, 5 sisters of which 4 were carriers of the nail anomaly. The patient showed, besides the nail deformities, complete absence of the patellae. There were, in addition, severe deformities of both lower extremities. The other members of the family with anonychia were not examined but it is conceivable that some may have shown absence of the patellae.

Firth[4] in 1912 reported the case of a family in which the mother and 3 children, all girls, showed congenital absence of the patellae and deformity of the nails. The mother, aged thirty-two, showed no patellae and deformed nails. The eldest daughter, aged ten, showed, in addition to these deformities, inability to fully extend the arms at the elbow, while the youngest daughter showed the deformities but was unable to fully extend only the left arm at the elbow. The third daughter, aged three and a half, showed a rudimentary patella on the left while the right was present and appeared normal. Twins and 2 siblings in the same family, all dead, were said to have been normal. An addendum to Firth's article mentioned a family reported by Dr. John Thomson, consisting of a father, mother and 9 children. The mother and 5 of the children showed complete absence of both patellae and deformity of all the finger nails and toe nails. The father and 4 other children were quite normal. The mother showed some slight inability to straighten her right elbow completely and she could not freely supinate her right forearm. The family reported by Rubin[14] consists of 3 members—a mother with no thumb nails and patellae of about one-half normal size, a son with no patellae but normal thumb nails and a daughter with no patellae but with thumb nails partly developed.

Trauner and Rieger[19] emphasize the dom-

* From the Departments of Radiology and Medicine of the Jewish Hospital of St. Louis, St. Louis, Mo.
† Captain, Medical Corps, Army of the United States.

inance of luxation of the head of the radius in their report of 6 members in four generations in which they found the following to be closely associated with each other: luxation of the head of the radius caused by hypoplasia or complete absence of the capitate eminence of the humerus, flexion contractures of various fingers, discoloration and incomplete development of the nails of the thumb, index fingers and the first and second toes. In 1 case, there was hypoplasia of the patella. In 1928, Aschner[1] collected from the literature the history of 8 families in which congenital defect or hypoplasia of the patella was inherited through several generations. Among the 8 families, there were 3 in which the bone defect was associated with a hereditary defect of the thumb nails in all the reported affected members of the family.

A complete study is reported by Oestereicher[11] of a family in which out of 21 members in five generations, 11 were carriers of the defective triad involving the nails, patellae, and elbow joints. There was a defect of the thumb nail in all affected members while 2 showed, in addition, involvement of the other nails. There was a patellar defect in 9 of the affected cases, while in the remaining 2 the information was incomplete in this regard. The anomaly of the elbow was present in 7 of the affected cases, in 2 the information was incomplete, in 1 only the right elbow was involved while in the last case the anomaly was completely absent.

Turner[20] in 1933 reported a study of 2 families in which 35 out of 79 persons were affected by the hereditary triad, namely, dystrophy of the nails, defect or severe hypoplasia of the patella, and deformities of the elbow. In the first family, every member showing dystrophy of the nails suffered also from the other two features, a total of 26 out of 39 persons being affected. In the second family, 27 of 41 persons suffered from dystrophy of the nails while only 9 suffered from the arthrodysplasias. At about the same time, Rutherfurd[15] described a hereditary complex occurring in 5 cases in three generations, characterized by recurrent dislocation of the patella, hereditary knock knee, and aplasia of the nails of the fingers and toes. In 1936 Lester[6] made a supplementary report on the family originally described by Firth in 1912. At this time the family had increased to three generations, of which 7 members of 13 show the deformities. To the relatively constant triad he adds a deformity of the ilium and thickening with convexity of the lateral border of the scapulae. A leaf-shaped discoloration of the iris was observed in a few of the cases.

In 1937, Montant and Eggermann[8] described a hereditary syndrome characterized by hypoplasia of the patellae, malformation of the radius and hemi-atrophy of the nails of the thumbs. These affections were discovered incidentally in an individual who presented herself at the clinic for some trivial unrelated complaint. The genealogical tree was charted when the patient gave the history that several of her ancestors and relatives presented similar malformations. In this way it was possible to determine that in five generations, 10 members of 30 were affected. The authors have emphasized the association of these malformations with the presence of light blue eyes and blond hair, and feel that this is a hereditary affection of a dominant character which is not sex linked. A constant feature in these cases was that only the nail of the thumb was affected and always in the same manner, namely, a hemiatrophy of the cubital side. All cases had a very marked hypoplasia of the patellae, never a complete absence.

Sever[17] reported the case of an elderly man in whom it was discovered, during the course of a routine physical examination, that the patellae were small and located on the external aspect of both knees. It was later observed that the nails on each thumb were rudimentary, while the remaining nails appeared normal. Roentgenograms of the elbow showed various bony exostoses about the joint, but it was not possible to determine the presence of any

FIG. 1. Hands of patient showing the involvement of the nails of the thumb and index fingers. The nails of the middle and ring fingers are slightly thinner than normal and somewhat flattened. The nails of the little fingers are entirely normal.

luxation, in view of the marked bony overgrowth. On questioning this patient further, it was learned that 2 nieces of his wife and a nephew had rudimentary nails on all fingers, but so far as the patient knew their knees were normal. On his mother's side, a niece and an uncle also had rudimentary nails on all fingers but nothing was known about their knees. The patient died of a cancer of the pancreas and Venable[21] performed an anatomical dissection of the right knee joint which is completely described in a recent report.

Although there has been some variation in the nature and degree of the congenital defects which have been described by the above authors, the localization of the abnormalities to the nails, particularly of the thumbs, to the patellae and to the elbows has been fairly striking. Characteristically, the disorder of the nails has varied from total absence of the nail to one that is only a little thinner than normal, always affecting more severely the thumb nail and becoming less marked toward the little finger. The typical dystrophic nail presents a small normal appearing base that is much thinner than normal and that gradually disappears about half way down the nail bed, allowing the fleshy end of the finger to turn backward over the nail (Fig. 1). Montant and Eggermann have emphasized the fact that only the nail of the thumb was affected and in a characteristic manner, namely, a hemiatrophy of the cubital side. In other cases, there has been complete absence of the nail of the thumb, with or without associated affection of the remaining fingers or, very occasionally, the toes.

The deformity of the patella has been characterized by total absence or at least severe hypoplasia of the patella. The knees appear flat when extended, square and angular when flexed (Fig. 2). The hypoplastic patella, when present, was located on the external aspect of the knees, lying rather high. The tubercle of the tibia is markedly prominent, as is also the internal condyle of the femur. There is genu valgum in some cases. The affected elbow shows an unusually prominent internal condyle, with an increased carrying angle (Fig. 3). The

FIG. 2. Knees of patient in flexion showing the square, angular appearance. The nail on the big toe of the right foot shows a suggestive deformity similar to the nails of the thumbs.

forearm cannot be fully extended and supination is limited. Roentgenograms of the elbow show an arthrodysplasia characterized by an elongation and deformity with luxation of the proximal end of the radius. The head of the radius is poorly formed and the superior radio-ulnar articulation is dysplastic (Fig. 4). In other cases there is extensive overgrowth of bone in the region

Fig. 3. Photograph of patient standing showing the prominent internal condyles of the lower end of the humeri and the exaggerated carrying angle. The extended knees appear flat with no suggestion of a patella. The hands are held in a pronated position.

of the elbow with secondary arthritic change.

Other less constant and variable features have been stressed by individual authors. Turner[20] called attention to the thick ankles with unusually large malleoli, particularly the internal malleolus. He emphasized the prominence of the acromial ends

Fig. 4. Roentgenograms of the left elbow showing the deformity of the proximal end of the radius and the dysplasia of the proximal radio-ulnar articulation.

of the clavicle, the undersized scapulae, and the small coracoid and acromial processes. In the hip and pelvis there is said to be an increase in the angle between the neck and shaft of the femur, with an increase in the normal concavity of the external surface of the ilium, giving the crest the appearance of an outward flare in its posterior half. Lester,[6] in addition to the constant triad, called attention to a leaf-shaped discoloration of the iris, an increase in the normal

Fig. 5. Lateral roentgenograms of both knees showing complete absence of the patellae.

concavity on the external surface of the ilium so that the crest seems to be increased posteriorly, and to minor changes in the shoulder girdle. Turner, and Montant and Eggermann noted with variable frequency a great laxity of the metacarpophalangeal and interphalangeal joints so that it is sometimes possible to hyperextend the digits of the hand until an angle of 90 degrees is formed with the back of the hand without discomfort to the patient.

knee, the shoulders, wrists, hands, hips and knees. During the course of the examination the deformity of the nails was noted as well as the evidence of total absence of the patellae. Roentgenograms of the knees and the elbow confirmed the clinical suspicion of total absence of the patellae, and established the presence and nature of the arthrodysplasia of the elbow joints (Fig. 4 and 5). The genealogical tree showed that a great-great-grandfather who lived in the eighteenth century is known to have had this affection. The line was apparently negative

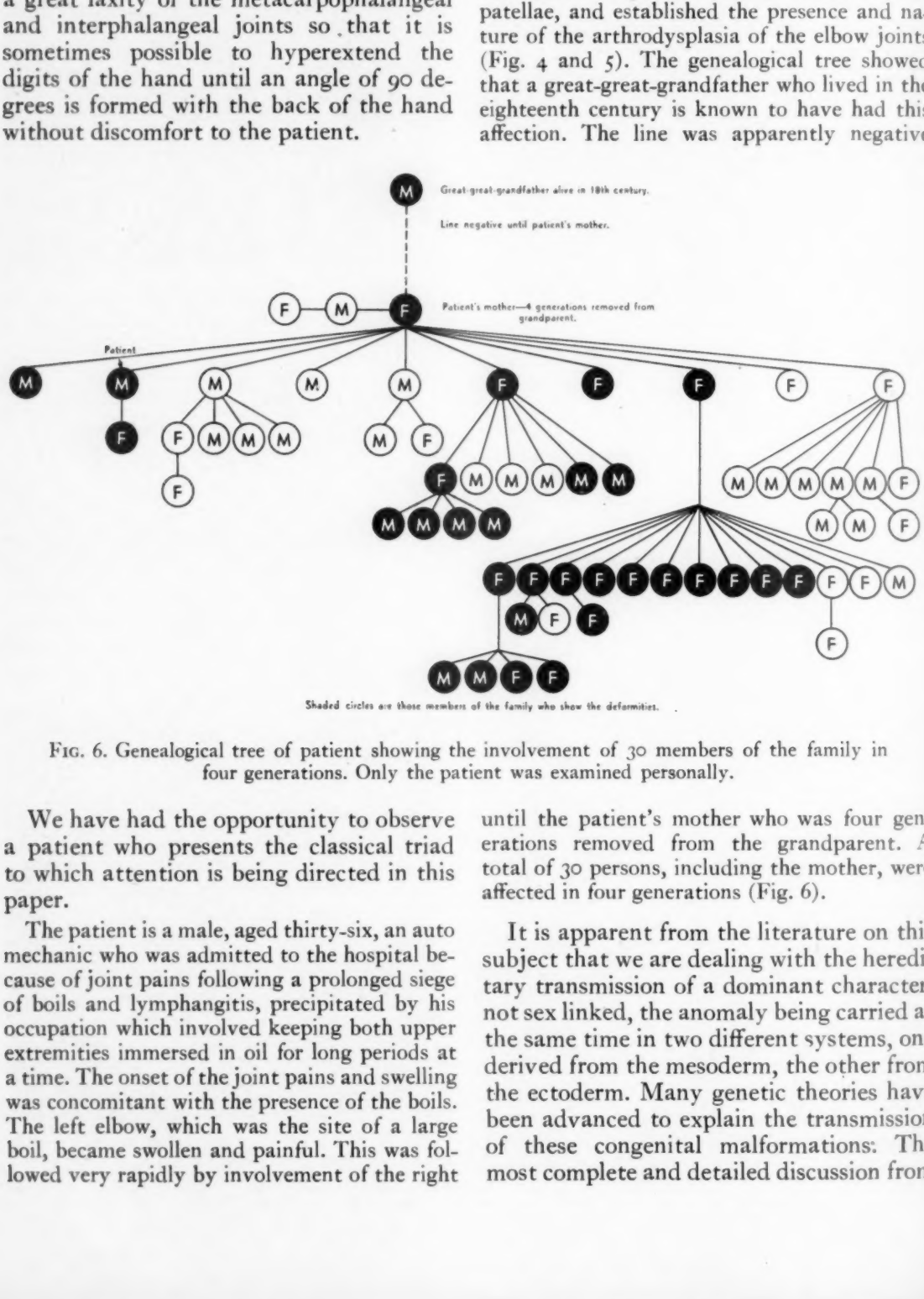

Great-great-grandfather alive in 18th century.
Line negative until patient's mother.
Patient's mother—4 generations removed from grandparent.
Patient
Shaded circles are those members of the family who show the deformities.

FIG. 6. Genealogical tree of patient showing the involvement of 30 members of the family in four generations. Only the patient was examined personally.

We have had the opportunity to observe a patient who presents the classical triad to which attention is being directed in this paper.

The patient is a male, aged thirty-six, an auto mechanic who was admitted to the hospital because of joint pains following a prolonged siege of boils and lymphangitis, precipitated by his occupation which involved keeping both upper extremities immersed in oil for long periods at a time. The onset of the joint pains and swelling was concomitant with the presence of the boils. The left elbow, which was the site of a large boil, became swollen and painful. This was followed very rapidly by involvement of the right

until the patient's mother who was four generations removed from the grandparent. A total of 30 persons, including the mother, were affected in four generations (Fig. 6).

It is apparent from the literature on this subject that we are dealing with the hereditary transmission of a dominant character, not sex linked, the anomaly being carried at the same time in two different systems, one derived from the mesoderm, the other from the ectoderm. Many genetic theories have been advanced to explain the transmission of these congenital malformations. The most complete and detailed discussion from

the genetic point of view is that of Aschner.[1] She has demonstrated that each of the anomalies can occur independently or in variable combinations with the other two. A defect of the patella can occur independently without involvement of the nails or the elbow joints (Little,[7] Aschner[1]). Hereditary dystrophy of the nails in the absence of skeletal anomalies has been sporadically reported (Tobias,[18] Jacobsen,[5] Pires Da Lima,[12] Ebstein,[3] Murray,[10] Chilton[2]). The hereditary occurrence of luxation of the head of the radius has been described as an isolated anomaly (Servier,[16] Princetau,[13] von Sury[22]). For these reasons, she concluded that there must exist three separate pathologic factors which are closely linked, as the three defects are inherited together with few exceptions. Since the whole syndrome does not occur quite so often as the association of the defect of the nails and the patella, it can be assumed that there is a closer linkage between these two genes in order to explain their frequent occurrence together and their inheritance together as if they were one factor. The genes for the defect of the patella and the thumb nail are not only linked together in the same chromosome, but are even very near neighbors to each other within the same chromosome. The gene for the luxation of the head of the radius is probably in the neighborhood of the other two genes, but not quite as close in the chromosome, as the whole syndrome does not occur quite so often as the association of the defect of the thumb nail and the patella.

Turner[20] postulated that since in neither family in his cases does the arthrodysplasia appear independently of the dystrophy of the nails, although the reverse occurs frequently, the factor for dystrophy of the nails must be present for the factor of the arthrodysplasia to be active. On the other hand, it is possible that both factors are present in every individual showing the dystrophy of the nails, but that a third factor is present also in those who do not show the arthrodysplasia, and the third factor acts as an inhibiting force on the arthrodysplsia or on the interaction of the two. Montant and Eggermann[8] concluded that a single gene is involved in the origin of the different anomalies. This is the concept of polyphenia, which assumes the origin of three different anomalies from a single dominant gene. Trauner and Rieger[19] and Oesterreicher[11] concurred in this assumption.

SUMMARY

An inherited congenital developmental defect involving the ectodermal and mesodermal layers of the embryo is described. The malformations affect, with striking consistency, the patellae, the nails of the hands, particularly of the thumbs, and the elbow joints. This triad is transmitted as a hereditary dominant character and is not sex linked. A case is described showing the typical clinical and roentgenologic appearance, in whose family tree a total of thirty persons in four generations are thus similarly affected.

Acknowledgment is made to Dr. Emanuel Sigoloff, of St. Louis, for authorization to make complete use of the records in this case.

REFERENCES

1. Aschner, Berta. Typical hereditary syndrome; dystrophy of nails, congenital defect of patella and congenital defect of head of radius. *J. Am. M. Ass.*, 1934, *102*, 2017–2020.
2. Chilton. Cited by Montant and Eggermann.[8]
3. Ebstein, E. Angeborene familiäre Erkrankungen an den Nägeln. *Dermat. Wchnschr.*, 1919, *68*, 113–124.
4. Firth, A. C. D. Congenital absence of patellae and deformity of nails in a mother and three children. *Proc. Roy. Soc. Med.*, 1911–1912, *5* (Sect. Stud. Dis. Child.), 44.
5. Jacobsen, A. W. Hereditary dystrophy of hair and nails. *J. Am. M. Ass.*, 1928, *90*, 686–689.
6. Lester, A. M. Familial dyschondroplasia associated with anonychia and other deformities. *Lancet*, 1936, *2*, 1519–1521.
7. Little, E. M. Congenital absence or delayed development of patella. *Lancet*, 1897, *2*, 781–784.
8. Montant, R., and Eggermann, A. Hereditary syndrome characterized by hypoplasia of patellae, malformation of radius and hemiatrophy of nail of thumb. *Presse méd.*, 1937, *45*, 770–772.

9. Most, A. Ein Fall von congenitalen Bildungsanomalien: intrauterine Belastungsdeformitäten der unteren Extremität; Anonychia und Onychatrophia congenita. *Allg. med. Centr.-Ztg.*, 1903, *72*, 153.
10. Murray, F. A. Congenital anomalies of the nails. *Brit. J. Dermat. & Syph.*, 1921, *33*, 409–412.
11. Oesterreicher, W. Gemeinsame Vererbung von Anonychie beziehungsweise Onychatrophie, Patelladefekt und Luxatio radii. Dominantes Auftreten in 5 Generationen. *Ztschr. f. d. ges. Anat.*, 1930, *15*, 465–476.
12. Pires Da Lima, J. A. Cited by Montant and Eggermann.[8]
13. Princetau. Cited by Aschner.[1]
14. Rubin, G. Congenital absence of patellae, and other patellar anomalies in three members of the same family. *J. Am. M. Ass.*, 1915, *64*, 2062.
15. Rutherfurd, W. J. Hereditary knock-knee, with recurrent dislocation of patella and aplasia of nails on fingers and toes. *Brit. J. Child. Dis.*, 1933, *30*, 34–38.
16. Servier. Cited by Aschner.[1]
17. Sever, J. W. Hereditary arthrodysplasia associated with dystrophy of the nails. *New England J. Med.*, 1938, *219*, 87–89.
18. Tobias, N. Hereditary familial dystrophy of the nails. *J. Am. M. Ass.*, 1925, *84*, 1568–1569.
19. Trauner, R., and Rieger, H. Eine Familie mit 6 Fällen von Luxatio radii congenita mit übereinstimmenden Anomalien der Finger- und Kniegelenke, sowie der Nagelbildung in 4 Generationen. *Arch. f. klin. Chir.*, 1925, *137*, 659–666.
20. Turner, J. W. Hereditary arthrodysplasia associated with hereditary dystrophy of the nails. *J. Am. M. Ass.*, 1933, *100*, 882–884.
21. Venable, J. H. Structure of a knee joint in hereditary arthrodysplasia. *South. Surgeon*, 1940, *9*, 345–350.
22. von Sury, K. Cited by Aschner.[1]
23. Wolf. Zwei Fälle von angeborenen Missbildungen; angeborener Mangel beider Kniescheiben. *München. med. Wchnschr.*, 1900, *47*, 766–777.

Vol. 51, No. 3

OSSEOUS ABNORMALITIES OF THE THORACIC CAGE SEEN IN FORTY THOUSAND CONSECUTIVE CHEST PHOTOROENTGENOGRAMS*

By MAJOR LEWIS E. ETTER, M.C.
MEDICAL CORPS RESERVE

THE literature on congenital and developmental defects and abnormalities of the thoracic cage is limited. Very little has been written in the radiological journals of this country on the subject, but a number of interesting articles have appeared in foreign publications.[3,4,7,10,11] The roentgenologist meets with these conditions in his daily routine and takes them as a matter of course, reflecting, perhaps, on the infinite variety of biological phenomena.

Of interest chiefly from the standpoint of anatomy, very little was known of the occurrence of thoracic anomalies until the advent of roentgenography. Identification of structural variations by dissection would be a tiring task and this accounts for lack of data on the subject in the anatomical literature and standard texts. The roentgenologist is interested in the abnormalities both from the anatomic and roentgenologic aspect since they at times may simulate pathological conditions as, for example, the mistaking of a bifurcated rib deformity for the wall of a tuberculous cavity. This may seem trite, but it is a fact that the mistake has been made.

While every roentgenologist is familiar with the more common anomalies of the thoracic cage, these are not of such frequent occurrence as to be an every day happening in the average practice. In fact, our statistics on the abnormalities herewith reported would indicate the conditions cited to be rare. Account must also be taken of the fact that this report deals with a segment of the male population of military age, and may therefore be found at variance with statistics accumulated in a study including both sexes.

But up to this time, with the exception of the reviews published by Ashbury,[1] and Ashbury, Whildin and Rogers,[2] no large series of cases giving these data have been reported. Inasmuch as our statistics and those of the authors quoted are substantially in agreement, it is felt that our figures represent a true picture of the occurrence of the various abnormalities which are shown in the accompanying tabulation (Table 1).

COMMENT

The occurrence of cervical ribs in this series, namely once in 600 men, may seem small, but we have held strictly to the following criteria in diagnosing cervical ribs: First, the rib must arise from the seventh cervical vertebral transverse process which is seen to project horizontally from the spine in contradistinction to the transverse process of the first dorsal vertebra which extends diagonally upward from the point of origin (Fig. 1), and second, it must have no connection anteriorly with the manubrium sterni although it may form a synostosis with the first rib (Fig. 4). Many ribs, which at first glance appear to be supernumerary, are found to be rudimentary first ribs when the above criteria are applied. It is of interest that in this series only one of the cervical ribs was found to be jointed (Fig. 2). Vinogradov[12] described 6 cases in which a joint appeared in the mid-portions of cervical ribs. Further, it should be stated that none of the individuals possessing these ribs had any symptoms referable to them at the time of the examination.

Considerable interest has been shown in the appearance of an anomaly of the first rib (Fig. 3) occurring usually in its mid-

* From the Medical Examination and X-Ray Sections, Armed Forces Induction Station, Altoona, Pennsylvania.

Fig. 1. Bilateral cervical ribs showing origin from horizontal transverse process of seventh cervical vertebra.

portion, and having the appearance of a healed fracture or pseudarthrosis. The accompanying figure shows one case in which the condition was bilateral. When this was first encountered we tried to get a history of injury because of the appearance of callus in a healing fracture, but in all cases the history has been negative. Upon first

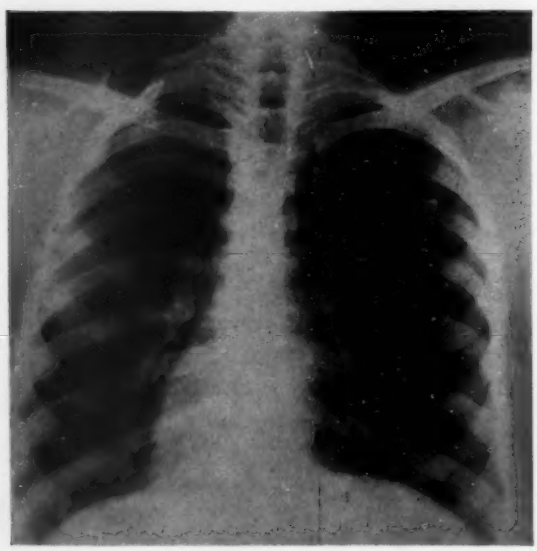


Fig. 2. Bilateral cervical ribs, the left one jointed.

study of a roentgenogram showing this abnormality one is struck by its similarity to a calcified tuberculous process at the apex of the lung. Upon closer examination, and a negative history of trauma, it be-

Table I

BONY ABNORMALITIES OF THORACIC CAGE IN 40,000 CHEST PHOTOROENTGENOGRAMS

		Right	Left		No. of Cases
Cervical ribs		12	14	26	
		Bilateral		41	
		Bilateral, one jointed		1	68
Anomalous first ribs		12	18	30	
		Bilateral		1	31
Rudimentary ribs	1st ribs	25	42		
	2nd ribs	3	2		
	3rd ribs	2	2		
	4th ribs	0	1		
	5th ribs	0	2		
		30	49		79
Synostosis of ribs	1– 2 ribs	46	31		
	2– 3 ribs	2	2		
	3– 4 ribs	2	1		
	4– 5 ribs	1	3		
	5– 6 ribs	6	2		
	6– 7 ribs	0	2		
	7– 8 ribs	1	1		
	8 –9 ribs	0	1		
	9–10 ribs	2	1		
		60	44		104
	Multiple synostoses				1
	Synostosis rt. cervical and rt. 1st rib				2
	Bilateral synostosis 1st and 2nd ribs				2
Bifid ribs	1st ribs	4	12		
	2nd ribs	3	2		
	3rd ribs	41	23		
	4th ribs	60	33		
	5th ribs	29	18		
	6th ribs	12	5		
	7th ribs	4	4		
		153	97		250
Bilateral bifid ribs	3rd	5			
	4th	2			7
Rib resection (drainage for empyema)					35
Skeletal deformity (scoliosis)					126
Healed fractures of ribs					48
Osteomyelitis of rib					1
Osteochondromatosis					1

comes clear that the lesion is an anomalous pseudarthrosis. Hallermann[5] described a case and drew attention to the appearance suggesting a healed fracture. Pickhan[9] also reported on this condition and conjectured on its possible phylogenetic connec-

tion by showing that similar joints occur in the upper ribs of the European crane.

In this series the most common rudimentary rib was found to be the first. Probably this is the reason that they are sometimes mistaken for cervical ribs although application of the criteria above given for cervical ribs will serve to differentiate the two. None of the individuals we saw had any symptoms from this anomaly, but a case has been reported by Henry[6] in which pressure of a rudimentary left first rib on the cervical sympathetic chain and stellate ganglion produced thermal changes in the left arm relieved by resection of the rib. Cases have also been reported[3,11] where aplasia of three or more ribs has caused deformities of the thoracic wall with eventration of the viscera.

Fig. 3. Bilateral anomaly of first ribs having appearance of healed fracture or pseudarthrosis.

Synostoses of the ribs were found more commonly on the right side than on the left side involving the right first and second ribs most frequently. It is interesting to note that synostoses were found to occur, both anteriorly and posteriorly, between all the ribs visible on the chest roentgenogram. One case only showed multiple synostoses (Fig. 4) in addition to bilateral cervical ribs, the right one of which formed a pseudarthrosis with the first rib. Clinically this man showed straightening of the dorsal spine with slightly limited mobility, but had no functional incapacity. An occasional synostosis had the appearance of a joint between the ribs (Fig. 5). A report of

Fig. 4. Multiple synostoses and bilateral cervical ribs, the right one forming a synostosis with the first rib (pseudarthrosis).

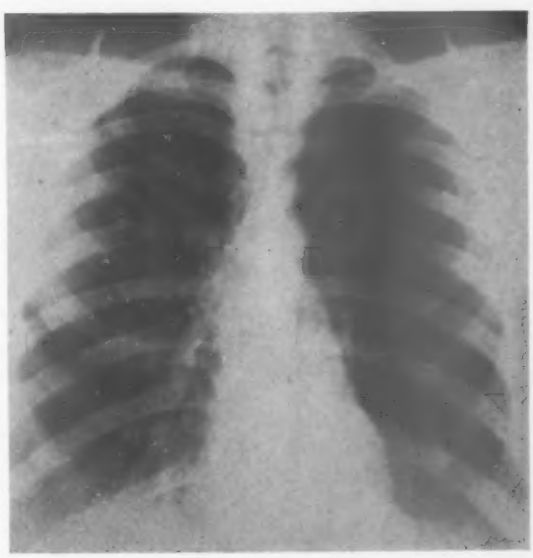


Fig. 5. Synostosis between right fifth and sixth ribs posteriorly, having appearance of a pseudarthrosis.

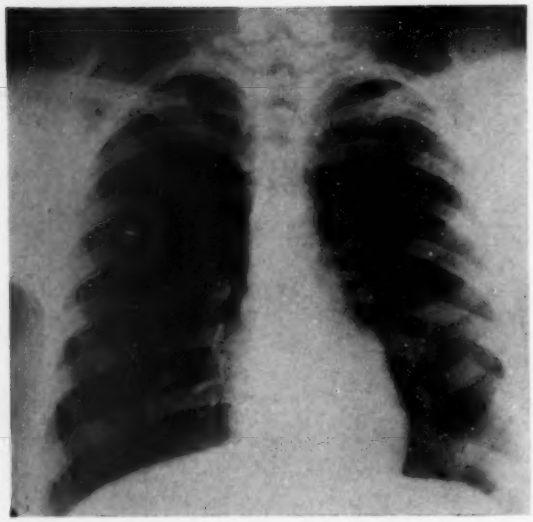


Fig. 6. Synostosis between left seventh and eighth ribs posteriorly suggesting appearance of an air cyst.

a case[8] in which there was complaint of pain from a lump beneath the left clavicle was found to be a pseudarthrosis between the end of the left first rib and the mid-portion of the second rib. Occasionally a synostosis may give rise to an appearance suggesting a pathologic process as shown in the accompanying roentgenogram (Fig. 6). Here a combination of shadows suggests an emphysematous bulla or air cyst at the left base. None of the men we saw had any symptoms or external evidence of synostosis of the ribs.

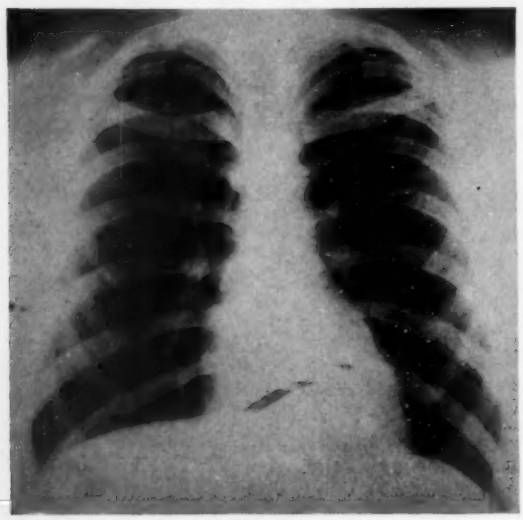


Fig. 7. Bilateral bifid third ribs.

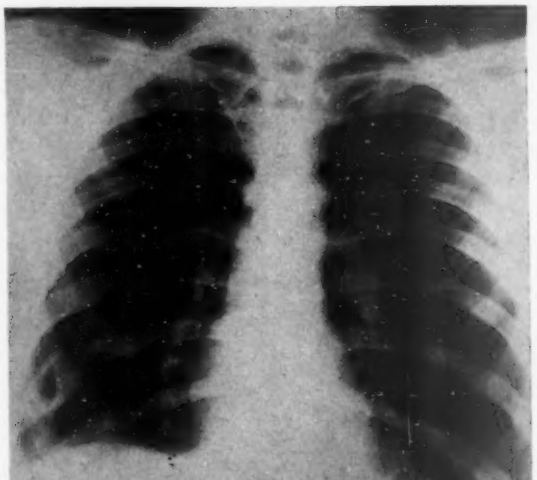


Fig. 8. Frequent appearance of rib produced by healed resection for empyema.

Bifid ribs showed the appearance of a lobster claw, occasionally incomplete; simple forking, and spatula forms. Their oc-

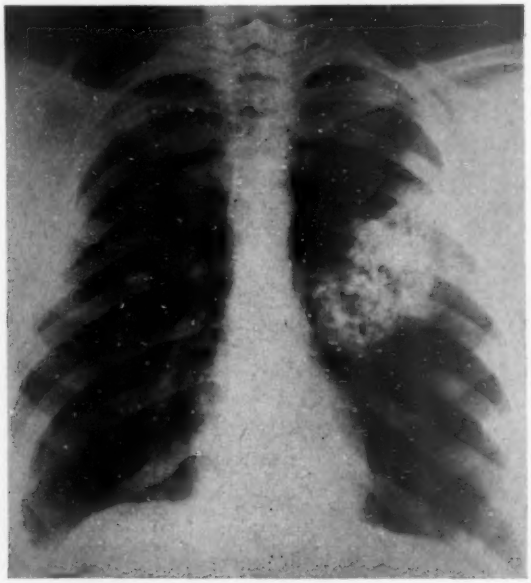


Fig. 9. Osteochondromatosis of ribs producing an appearance suggestive of massive healed primary tuberculosis.

currence was 50 per cent more on the right side than on the left side. The right fourth rib showed this anomaly most frequently. Bilateral bifid rib occurred rarely, only 7 cases being found in the series (Fig. 7).

Scoliosis of acceptable degree by Army standards; that is, less than 2 inches' deviation from the midline, on a postural basis, was noted infrequently, namely 1 in 300 men.

Healed fractures of ribs were seen only once in 800 men and ribs resected for empyema once in 1,100. The appearance produced by healed resection for empyema was fairly constant (Fig. 8) and usually showed a lacunar defect in a spindle-shaped deformity of the rib.

In one case a very unusual appearance was presented by osteochondromatosis. Upon first viewing the roentgenogram (Fig. 9) the appearance was that of a massive healed primary tuberculosis, but lateral views showed the connection anteriorly with the ribs and costal cartilages. A bone survey then was done and showed typical osteochondromata of the long bones.

SUMMARY

The statistical data of the occurrence of osseous abnormalities of the thorax have been tabulated and attention drawn to the rare conditions which may possibly be mistaken for pathologic processes.

The author expresses his thanks to Cpl. John J. White for his valuable assistance in the preparation of the statistical data.

REFERENCES

1. Ashbury, H. E. Roentgenological report of chest examinations made of registrants at U. S. Army Induction Station No. 6, Third Corps Area, Baltimore, Maryland, period ending April 30, 1941. Am. J. Roentgenol. & Rad. Therapy, 1941, *46*, 241–244.
2. Ashbury, H. E., Whildin, J. G., and Rogers, F. T. Roentgenological report of chest examinations made of registrants at U. S. Army Induction Station No. 6, Third Corps Area, Baltimore, Maryland, May 1, 1941, to March 31, 1942. Am. J. Roentgenol. & Rad. Therapy, 1942, *48*, 347–351.
3. Buot, H. F. Contribution à l'étude des aplasies costales. Paris, 1934.
4. Dreyfus-Le Foyer, P., Augé, and Brunet, C. Anomalie par défaut de la première côte. *Ann d'anat. path.*, 1936, *13*, 1028–1030.
5. Hallermann, W. Ueber Anomalien der ersten Rippen. Waldkirch i.b., Freiburg, 1935.
6. Henry, C. K. P. Case of congenital malformed first dorsal rib. *Canad. M. Ass. J.*, 1936, *34*, 545–547.
7. Kienböck, R. Ueber angeborene Rippenanomalien. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 1908–1909, *13*, 269–298.
8. Levi, D. Fusion of middle third of first and second ribs. *Proc. Roy. Soc. Med.*, 1932, *25*, 1233.
9. Pickhan, A. Beiträge zur pathologischen Osteologie. *Röntgenpraxis*, 1930, *2*, 969–976.
10. Simon, S. Zur Kenntnis der Rippenanomalien im Kindesalter. *Röntgenpraxis*, 1938, *10*, 45–50.
11. van der Molen, H. J. Two cases of anomalous ribs, one combined with spina bifida. *Maandschr. v. kindergeneesk.*, 1937, *6*, 209–213.
12. Vinogradov, V. Jointed cervical ribs. *Siberian Arch. Med.*, 1929, *4*, 510.

RATIONALE AND RESULTS OF ROENTGEN TREATMENT OF THE ADRENAL GLANDS IN ANGINA PECTORIS*†

By W. RAAB, M.D., *and* A. B. SOULE, JR., M.D.
BURLINGTON, VERMONT

RATIONALE

THE syndrome of angina pectoris is generally recognized as being caused by a state of acute anoxia of the heart muscle (Keefer and Resnik, Levy, *et al.*). The presence of coronary sclerosis *per se* does not suffice to explain the characteristic acuteness of the anginal attacks.

The common conceptions of acute "coronary spasms" or acute "hemodynamic strain" are not satisfactory. Coronary spasms have never been directly observed. They were only hypothetically postulated for the purpose of explaining the clinical manifestations of acute myocardial anoxia. Moreover, such spasms are the less likely to occur, the more rigid the sclerotic coronary arteries grow. The pain-relieving effect of the vasodilating nitrites cannot be accepted as positive evidence of a preexisting spasm of the coronary vessels if the possibility of a primarily biochemical mechanism of acute myocardial anoxia is taken into consideration. Furthermore, there is no evidence of an increased hemodynamic strain as being a regular feature in angina pectoris. On the contrary, blood pressure and pulse rate may even be lower during attacks than during the interval (Raab[a]).

Shambaugh and Cutler were the first to discuss the possibility that adrenalin discharges may be involved in the pathogenic mechanism of angina pectoris. The theory advanced by one of us (Raab[b]) that anginal attacks are brought about by the acutely anoxiating effects of adrenalin discharges upon a heart muscle whose coronary arteries are sclerotic and thus unfit for adequate compensatory dilatation is based upon the following facts:

(1) Adrenalin exerts a specific, intensely anoxiating effect upon the heart muscle (Barcroft and Dixon, Evans and Ogawa, Gremels, Rein, and Green and his coworkers) which by far exceeds the oxygen requirement for the simultaneous increase of hemodynamic action (Gollwitzer-Meier, Kramer and Krüger).

(2) Adrenalin is physiologically discharged from the adrenal glands into the blood stream under the influence of physical exercise, emotions, cold (Cannon, *et al.*), under the very conditions which usually elicit anginal pain.

(3) The heart muscle possesses a greater tendency than other tissues to accumulate circulating excess amounts of adrenalin, and likewise accumulates other adrenal catechols (Raab[c,e]).

(4) During physical exercise or exposure to cold the adrenalin content of the heart muscle increases (Fig. 1) while that of the adrenal glands diminishes (Raab[c,e]).

(5) Injection of adrenalin is likely to produce anginal symptoms in persons with coronary sclerosis (Levine, Ernstene and Jacobson; Katz, Hamburger and Lev; Cottrell and Wood) and, if given in large doses, also in healthy persons (Wenckebach, (Raab[b], self-experiment).

(6) Abnormally intense discharges of adrenalin into the blood stream during physical exercise were observed in all of 12 patients suffering from angina pectoris. They disappeared in all of 7 successfully treated patients in whom the tests were repeated after treatment (Raab[d]).

(7) The electrocardiographic changes which occur during anginal attacks are practically identical with those following the administration of adrenalin (Vesa,

* From the University of Vermont, College of Medicine, Divisions of Clinical Medicine and Roentgenology.
† This study was aided in part by a grant from the Rockefeller Foundation.

Lepeschkin, Katz, Hamburger and Lev, *et al.*).

(8) Patients with tumors of the adrenal medulla often suffer from anginal attacks (Bauer, Scherf, Nuzum and Dalton, Brunschwig, Humphreys and Roome, *et al.*) during which an increased adrenalin level was found in the blood (Brandt and Katz) and which disappear after removal of the adrenal tumor (Lenhartz).

(9) Conditions which are known to increase the secretion of adrenalin, such as tobacco smoking (Cannon, Aub and Binger; Eichholtz; Stewart and Rogoff; Kobro; Raab[7]) or overdosage of insulin (Brandt and Katz; La Barre and Houssa; Kugelmann; Raab[7]) or breathing of low oxygen concentrations (Cannon and Hoskins) are likely to elicit anginal symptoms (Külbs; Deneke; Strauss; Hadorn; Schönbrunner; Rothschild and Kissin; Levy, *et al.*).

Large doses of roentgen rays applied to the adrenal region of animals have been found to be followed by structural changes of the adrenal glands (Harvey; Cottenot; von Decastello; Grabfield and Squier; Holfelder and Peiper; Martin, Rogers and Fisher; Tsuzuki; Desjardins; Engelstad and Torgersen). These changes concern chiefly the cortex, although the medulla was also found to participate in part of the experiments.

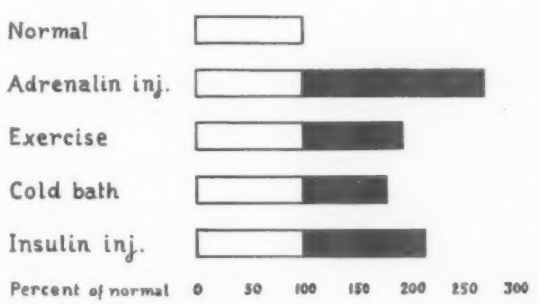


Fig. 1. Concentration of adrenalin and adrenalin-like substances in the heart muscle of the white rat. The white squares indicate the average normal concentration per gram of myocardial tissue; the black areas indicate the increase of hormonal material beyond normal under experimental conditions: Subcutaneous injection of 2.5γ of adrenalin per gram body weight; swimming in a pool for six to fifteen minutes; a cold bath of 5° C. for ten minutes; subcutaneous injection of an average of eight units of insulin.

Recent experiments carried out by us on rats showed that single doses of 100 and 1,000 roentgens caused only slight changes

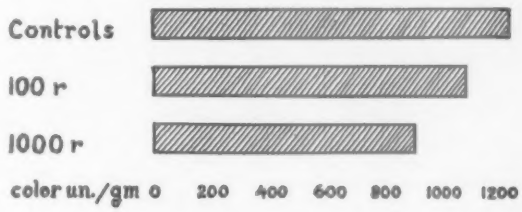


Fig. 2. Adrenalin plus adrenalin-like substances in the heart muscle of the rat following physical exercise (swimming in cold water). Two months after irradiation of the adrenal region with 100 and 1,000 r respectively the total concentration of the hormonal substances in the heart appears diminished, probably due to diminution of the excess influx of this material into the heart muscle which is normally taking place during exercise (compare Fig. 1) (Raab and Soule).

of the content of the adrenal glands in adrenalin and related catechols within two months. However, the accumulation of such hormonal material in the heart muscle following physical exercise was distinctly diminished two months after irradiation of the adrenal region (Fig. 2).

Desjardins, Frey, and Engelstad and Torgersen, in contrast to earlier investigators, reached the conclusion that the roentgen-ray sensitivity of normal adrenal glands is not greater than that of other tissues. However, the roentgen-ray sensitivity of living cells increases with the degree of their activity (Holzknecht's law) and the state of overactivity of the adrenal medulla and of its nervous secretory apparatus which seems to prevail in angina patients, as discussed above, makes the possibility of a beneficial, normalizing effect of roentgen treatment upon the adrenal glands of angina patients and upon their nervous supply plausible, even with a dosage which does not suffice to cause any damage to the glands.

The results of irradiation of the adrenal glands in 100 European patients with an-

TABLE I

IMPROVED CASES

Case No.	Age	Sex	Blood Pressure	Severity	Duration (yr.)	Electrocardiogram	Coronary Thrombosis (years ago)	Complications	Date of Treatment	Improvement		Other Medication after Roentgen Treatment
										Degree	Duration (mo.)	
1	54	♂	170/100	M	½	–	—	—	7/39	+++	45	Quinidine
2	47	♀	100/70	M	2½	+	—	—	10/39 5/40	++	32 11	—
3	50	♀	216/98	M	2	+	1	Spinal arthritis +	9/39	+++	42	—
4	58	♂	142/80	S	⅛	+	—	Temporary decompensation	10/39	+++ – +++	30 (1) 19	Digitalis
5	63	♂	160/80	M	8	–	—	—	5/40	++	36	—
6	54	♀	200/100	M	1	?	—	Temporary decompensation. Died 11/43	4/40 12/40	++ – + –	7 (2) 20 (13)	Digitalis
7	69	♂	118/80	M	3	+	—	Temporary decompensation. Br. asthma	4/40 1/41	++ ± +++	5 5 32	Digitalis
8	60	♂	175/96	M	5	++	—	Spinal arthritis ++	12/40 7/42	+++ ± ++ +++	12 1 6 17	—
9	47	♂	155/100	S	¼	+	—	Spinal arthritis +	12/40 4/41 +Th.*	+ +++	4 26	—
10	35	♂	166/78	L	1½	++	—	Hyperthyroidism	2/41	+++ ++ +++	11 7 8	—
11	71	♂	126/55	S	6	++	2 ½	—	2/41* 4/41* 11/41	+ ++ ++	2 7 18	Theocalcane
12	53	♀	190/106	M	14	+	14; 4		3/41	+++	26	—
13	59	♂	150/70	S	3	+	3	Temporary decompensation. Died 8/42	10/39 7/41	++ – ++ –	9 (11) 5 (9)	Digitalis
14	57	♀	170/86	S	2	++	—	Pernicious anemia. Spinal arthritis ++	6/41 8/41 +Th.	+ ++ +++	2 9 12	Liver extract
15	67	♂	210/110	S	6	?	—	Temporary decompensation Spinal arthritis +	9/39 4/40	++ – +++ ±	6 (½) 6 4	Digitalis
16	72	♂	156/80	M	6	+	—	—	3/41 12/41*	++ +	8 18	—
17	55	♂	148/86	M	1½	+	—	Spinal arthritis +	12/40* 2/41* 9/41 +Th.	– + +	(4) 13 10	—
18	56	♂	170/110	S	10	+	—	—	12/40 3/41	++ +++ ++	2 18 9	—

TABLE I—(*Continued*)

Case No.	Age	Sex	Blood Pressure	Severity	Duration (yr.)	Electrocardiogram	Coronary Thrombosis (years ago)	Complications	Date of Treatment	Improvement		Other Medication after Roentgen Treatment
										Degree	Duration (mo.)	
19	60	♂	160/88	L	4	+	—	—	3/41 3/42*	+++ ± +++	8 3 9	—
20	60	♂	160/86	S	½	—	½	Meteorism	7/41	+++ ++	2 20	—
21	56	♂	180/110	S	2½	+	½	Aerophagia Died 2/43	5/41 8/41*	– + ++ +++	(3) 4 6 8	Theobromine, quinidine
22	51	♀	166/80	S	2	+	—	Diabetes	7/41 9/41*	++ ++	2 20	—
23	72	♂	160/80	M	½	++	—	—	7/41	++ +	2 20	—
24	61	♂	160/90	M	12	?	—	—	5/40	+++ –	16 25	—
25	60	♂	140/100	M	3	+	—	—	7/41	++	22	Thiamine
26	58	♂	140/100	S	4	+	1½	Spinal arthritis +	10/41 7/42	++ ++	7 11	—
27	75	♀	176/90	M	3	+	2	Spinal arthritis +	12/41	+++ ± +++	6 2 16	Aminophylline
28	62	♂	130/82	M	1½	++	—	Died 8/41	1/41	+++	7	—
29	64	♀	220/112	S	2	++	—	Died 2/42	2/41	++ ?	5 (7)	—
30	63	♂	186/100	M	5	++	5	Died 2/43	3/42	++ +	4 2	—
31	75	♂	198/118	M	3	+	—	—	10/41 6/42	— ++	(7) 18	Theobromine

S = severe; M = medium; L = light.
* Treatments carried out in other places with supposedly the same technique.

gina pectoris have been published previously by one of us (Raab[5]). Seventy-six of these patients were either entirely freed of their complaints or at least improved for an average period of twelve and a half months, calculated until the time when further follow-ups became impossible for technical reasons.

In this country 42 typical angina cases have been examined and treated by us since July, 1939. Thirty-one of these were males, 11 were females.

As shown in Tables I and II, the cases were classified as severe (S: daily intense attacks brought about by slight exertion, etc., and also occurring at rest), medium (M: attacks less frequent or less intense and uncommon at rest) and light (L: attacks occurring only now and then or of a mild degree).

The technique of treatment consisted in a series of six single treatments on consecutive days; three to the left upper quadrant of the abdomen, posteriorly, and three to the right, the left and right areas being treated on alternate days. Two hundred roentgens, measured at the skin, were administered at each treatment. Thus, each

TABLE II

UNIMPROVED CASES

Case No.	Age	Sex	Blood Pressure	Severity	Duration (yr.)	Electrocardiogram	Coronary Thrombosis (years ago)	Complications	Date of Treatment	Improvement		Other Medication after Roentgen Treatment
										Degree	Duration (mo.)	
32	48	♂	140/100	S	8	++	—	—	3/41 6/41* 8/41*	— + —	(5) 2 (4)	—
33	66	♀	170/90	S	5	++	5 ½	Spinal arthritis ++	3/41 5/41 10/41 +Th.	— + —	(5) 1 (7)	—
34	60	♂	132/80	M	10	+	10 ½	—	11/41 3/42*	— —		—
35	34	♀	250/170	S	2½	+	—	Temporary decompensation	3/41 5/41	— —		Digitalis
36	58	♂	212/84	S	6	—	—	—	4/40 8/40	— —		—
37	63	♂	170/110	M	½	+	—	Spinal arthritis ++ Died 2/42	9/41 12/41	+++ + —	1 1 (3)	Theobromine
38	66	♂	126/66	M	4	—	—	—	3/41	+ —	2 (12)	—
39	52	♂	118/74	M	4	—	—	—	1/41	—		—
40	47	♀	124/62	M	4	+	—	—	3/41	++ —	1 (3)	—
41	64	♂	230/130	L	10	+	—	Paroxysmal tachycardia	1/41	—		—
42	55	♂	130/76	S	8	++	—	Thyroidectomy 6 yr. ago (B.M.R. −19%)	10/40	—		Thyroid

* Treatments carried out in other places with supposedly the same technique.

area was given 600 r as a total dose per series. The other technical factors were: 200 kv. (peak), 20 ma., 50 cm. target skin distance, 1.5 mm. Cu plus 1.0 mm. Al filter; size of fields 15 by 15 cm.

Several patients with evidence of associated hypertrophic spinal arthritis were given supplemental irradiations to the thoracic and cervical spine, a single dose of 200 r being administered to each involved area through a 10 by 15 cm. cone.

In a number of instances the series of treatments over the adrenal region was repeated either by the one of us (Soule) or by other roentgenologists in other places. When the latter was the case, it is indicated by asterisks in Tables I and II. The minimum intervals between two successive series of treatments were six to eight weeks.

RESULTS

Complete disappearance or marked improvement (+++) of the anginal symptoms for six to forty-five months occurred in 38 per cent of the 42 cases; another 33 per cent were considerably improved (++) from five to forty-three months; 3 per cent were only slightly improved (+), and 26 per cent remained unimproved (−). Among the latter 11 cases only 2 had received the full three series of treatments, and thus are to be qualified as definite failures.

In the improved cases the average number of series of treatments given was 1.6.

The duration of uninterrupted improvement ranged between five and forty-five months, with an average total duration of twenty-four months, up to date. Temporary complete relapses with the symptoms as intense as before treatment occurred in sixteen per cent of the improved cases, and complete relapses still continuing at the time of the patient's last report or ending in death in 10 per cent.

Blood pressure, electrocardiogram and other clinical features could not be followed as carefully as in the European material since most of the patients discussed in the present series had come for treatment from distant places and remained in contact with us only by correspondence.

In 8 hypertensive cases there was no significant change of the blood pressure despite a marked improvement of the anginal symptoms (average 175/81 before and 184/83 mm. Hg after treatment). The same had been true in the hypertensive European patients whose anginal complaints were improved.

In 6 cases a pathological electrocardiogram at rest showed partial or complete normalization. Electrocardiograms after exercise were not carried out in this series.

Eleven of the 31 improved cases continued the use of various drugs after the roentgen treatment, as indicated in Table 1, for varying periods of time.

In 7 cases in whom abnormally intense discharges of adrenalin proper and adrenalin-like substances (catechols) into the blood stream had been observed in connection with physical exercise, these discharges disappeared as soon as clinical improvement had set in (Fig. 3) and reappeared in 1 case during a relapse.

Death occurred in 7 of 42 patients treated within a period of four and a half years. Three of these (No. 21, 28 and 30) died suddenly during a state of clinical improvement, apparently from coronary occlusion; 2 cases (No. 21 and 28) had been practically free of anginal complaints for periods of several months until death. Three others (No. 6, 13 and 29) died during relapses of their anginal condition after temporary improvement; 1 patient (No. 37) who had been classified as unimproved died from pneumonia. In Case 13 an autopsy was performed. The medium sized coronary branches were sclerotic. The adrenal glands appeared normal grossly. Microscopically "the adrenal cells were well preserved. The cells of the zona fasciculata and the zona reticularis appeared unusually foamy." The kidneys showed signs of passive congestion and moderate atheromatosis of the arterioles.

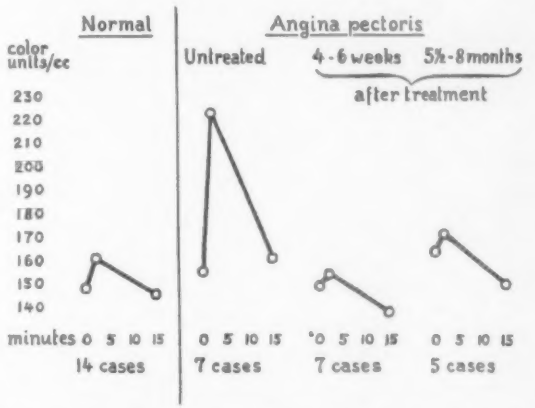


Fig. 3. Reaction of the blood level of adrenalin and adrenalin-like substances to a standard physical exercise test (climbing stairs) in normal persons and in angina patients before and after roentgen irradiation of the adrenal region (average curves).

(In a previous publication (Raab[4]) the figures given in these curves were interpreted as representing "adrenocortical compounds." Later investigations have shown, however, that cortical steroids do not participate and that the chromogenic material which is expressed in color units per cubic centimeter of blood consists essentially of adrenalin proper and of adrenalin-like catechols (Raab[9]).)

One patient who is not included in Table 1, a man aged forty, with severe attacks of only a few months' duration following a coronary occlusion, died two weeks after the first series of treatments from an occluding hemorrhage under the intima of the right coronary artery. The adrenal glands appeared normal at autopsy.

Most of the patients from out of town were questioned about their condition at repeated intervals. Since the subjective

Table III

	Patients Treated in Burlington (1939–1942) 42 cases		Patients Treated in Vienna (1936–1938) 100 cases	
	Improved	Unimproved	Improved	Unimproved
Number	74%	26%	76%	24%
Age	59 yr.	55 yr.	60 yr.	60 yr.
Males Females	74% 26%	73% 27%	84% 16%	87% 13%
Pathological electrocardiogram at rest	77%	73%	50%	30%
Coronary infarction before treatment	22%	18%	6%	1%
Spinal arthritis	22%	18%	20%	21%
Severe cases Medium cases Light cases	39% 55% 6%	46% 46% 8%	28% 58% 14%	50% 38% 12%
Duration of angina pectoris before treatment (average)	4 yr.	5½ yr.	3¼ yr.	5⅓ yr.
Systolic blood pressure (average)	164 mm.	164 mm.	154 mm.	172 mm.
Average duration of improvement	24 mo.	—	12½ mo.	—
Reported cardiac deaths*	14%	0%	1.3%	4%

* The discrepancy between the percentages of reported cardiac deaths in the American and the European cases may be due in part to the shorter total period of contact with the latter and the lack of further reports about their fate.

reaction of angina patients is the most decisive criterion of therapeutic results, some of the written answers received will be quoted in brief abstracts (the first and, if any, the second and third series of treatments will be indicated as *I, II, III*):

Case 1 (M): 34 months after *I:* "I can walk on even level. Cold weather does not affect me. . . . There is no comparison how much better I feel now than before treatment."—38 months after *I:* "I am happy to state that my last report still holds good."—46 months after *I:* "No change."

Case 2 (M): 32 months after *I:* "I feel very much better than before treatment but my breathing is very short. . . . I have made my own garden this year."—43 months after *I:* "I walk good now but slow, am better than before treatment."

Case 3 (M): 33 months after *I:* "Feeling fine and am not bothered with any pain."—43 months after *I:* "Feeling fine, everything OK."

Case 5 (M): 25 months after *I:* "If I move slowly and take my time in my work, my chest gives little trouble . . . cold weather didn't seem to affect the pain. . . . The treatment did give considerable relief."—37 months after *I:* "Am at present working every day, do not feel any pain unless I hurry. In cold weather I still get pains. . . . Condition better than before treatment."

Case 7 (M): 26 months after *I:* 16 after *II:* "I have no chest pain. . . . A great deal better than before treatment."—42 months after *I:* 32 after *II:* "Continually free of chest pain."

Case 8 (M): 19 months after *I:* "I rarely ever have any chest pains or distress, except when I indulge in over-eating. . . . It is my impression that the treat-

ments have given me great relief."—36 months after *I;* 17 months after *II:* "Glad to say that I am well."

Case 9 (S): 17 months after *I;* 13 after *II:* "No chest pain or distress, can walk and do other routine physical exercise." Work involved "continual walking, chopping brush, etc., and it was all carried out without distress."—30 months after *I;* 26 after *II:* "Improvement almost 100 per cent."

Case 10 (L): 16 months after *I:* "Decidedly improved. . . . Am able to do the routine work as a janitor but not to shovel snow, carry heavy loads up stairs, etc."—26 months after *I:* "No distress excepting one day when engaged in unusual physical activity. . . . Greatly improved."

Case 11 (S): 16 months after *I;* 7 after *III:* "I have been greatly improved. I only take a nitroglycerine tablet once or twice a month. I am able to do routine household duties with much greater ease. I can't walk well in windy or cold weather."—27 months after *I;* 18 after *III:* "I feel that my condition is good. . . . Much improved but still chest pain from cold and windy weather. Over-eating causes distress."

Case 12 (M): 15 months after *I:* "There is no comparison with the condition before treatment. . . . I find it a pleasure to walk and am able to climb stairs and come up the hill without any after effects. I am now able to do almost everything."—26 months after *I:* "Even further improved. Have been able to do all things with more ease."

Case 14 (S): 13 months after *I;* 11 after *II:* "Very much improved. . . . No chest pains. Am able to walk short distances, also to do my few household tasks. . . . A great deal of relief up to and including the present time."—23 months after *I;* 21 after *II:* "Much the same; much better than before treatments."

Case 16 (M): 13 months after *I;* 4 after *II:* "The treatments have given considerable relief. . . . I walk a mile or more each day. . . . Reactions to emotions and cold not so good. . . . Am decidedly better than before treatment."—26 months after *I;* 17 after *II:* "Not much further change." Altogether "considerably improved."

Case 17 (M): 16 months after *I;* 14 after *II:* "My condition is improved. . . . Still have daily manifestations, even though mild, of chest distress brought on by walking."—27 months after *I;* 25 after *II;* 18 after *III:* "No further change."

Case 18 (S): 12 months after *I;* 9 after *II:* "I feel a whole lot better than it was before the two treatments. I hunted deer five days and ran a trap line for three weeks . . . and have done a lot of walking and mountain climbing. . . . I couldn't have done these things a year ago or a tenth part of it."—29 months after *I;* 26 after *II:* "Working 60 hours a week on defense work in a machine shop. . . . Can walk miles if do not eat. . . . Most distress after supper. Walking uphill bad but very much better than before treatment."

Case 19 (L): 15 months after *I;* 3 after *II:* "I am infinitely better than before the treatments. They have greatly relieved my chest complaints. I can walk a dozen squares now . . . when I could not walk two before."—21 months after *I;* 9 after *II:* "Still much benefited by the treatment. . . . Have reactions after effort but as long as I am careful I am wonderfully well."

Case 20 (S): 11 months after *I:* "Condition better than before treatment. . . . At times there is a recurrence of the pains in the left shoulder but not nearly so frequently nor so severe."—22 months after *I:* "The same or perhaps slightly better." Altogether "most decidedly improved."

Case 21 (S): 13 months after *I;* 9 after *II:* "Am much better. . . . Attacks of chest pain increasingly fewer and much milder. I have had as much as two weeks on end of freedom from pain. Discomfort and pain spells after meals have almost completely disappeared. . . . Feel very happy about the wonderful improvement."—Died suddenly after 8 more months without attacks (according to letter from his widow).

Case 22 (S): 11 months after *I;* 9 after *II;* "My condition is much better than before treatment. . . . I just have a little trouble getting undressed and to lie down in bed. Just for a minute."—22 months after *I;* 20 after *II:* "I am doing swell. I even walk up and down stairs without trouble. . . . The treatments have given me wonderful relief."

Case 23 (M): 11 months after *I:* "Am much better than before the treatment. Can do light work if I start off gradually. Can walk leisurely, but not far at a time, without stopping to rest when I feel the chest pains."—22 months after *I:* "Much better than before treatment but cannot walk much or do anything strenuous, especially if cold and windy."

Case 25 (M): 10 months after *I:* "I am doing much better this year than last. I can walk better, eat better and do my work much easier."—22 months after *I:* "Better than before treatment, but cold bothers and pain if I exercise after meals."

Case 26 (S): 7 months after *I:* "I am much better. . . . Pain improved considerably. I can walk about a block before I begin to get pains. . . . Emotions, cold weather and meals seem to be about the same as before."—18 months after *I;* 10 after *II:* "Am suffering much less pain in chest."

Case 28 (M): 8 months after *I:* "I am working five days a week and am feeling very well. I walk a couple of miles a day and feel fine for it but a couple of times when the wind was blowing hard I felt a slight pain but it left right away." (Climbs 22 steps every hour 40 times a week).—Died suddenly one month later.

Case 29 (S): 5 months after *I:* "I am feeling much better now and by being careful do not suffer much pain."—Died 7 months later.

Case 30 (M): 4 months after *I:* "I am distinctly improved regarding pain. My ability to walk is distinctly improved."—7 months after *I:* "Still definitely better than before radiation therapy. . . . However pain of moderate severity is becoming more easily produced either by exertion or from emotional stress."—Died 5 months later.

Case 31 (M): 3 months after *II:* "Decided relief from chest complaints. . . . I have less pressure and with a pause now and then things get normal."—18 months after *II:* "Feel fairly good. Got employment as messenger, am out of doors quite a bit."

Nine patients who had been incapacitated through their anginal symptoms resumed work: 2 as farmers (No. 5 and 7), 1 as a foreman in a factory (No. 28), 1 as a restaurant chef, later going into defense work (No. 18), 1 as a cook (No. 6), 1 as a civil engineer (No. 9), 1 as a minister (No. 21), 1 as a bookkeeper (No. 17) and 1 as a messenger at the age of seventy-six (No. 31).

DISCUSSION

The results of roentgen irradiation of the adrenal glands in angina pectoris in the above described series of American patients are similar to those obtained in Europe by one of us (Raab[b]) and by other investigators.

Hadorn (Berne) applied the method "in 12 cases of ambulatory angina pectoris, partly of the severest degree, which had been treated unsuccessfully for a long time. The effect was an immediate one in 7 cases." In 1 case a normalization of the electrocardiogram which had been persistently pathological for four years, accompanied the subjective improvement.

Lippross (Dresden) reports 4 cases with the conclusion: "In severest cases of status anginosus we achieved the best results with roentgen-ray irradiation of the adrenal glands as suggested by Raab."

Professor A. Schittenhelm, head of the Second Medical Clinic of the University of Munich writes: "My experiences are only limited but still of a kind that I would recommend under all circumstances radiation therapy to every patient with angina pectoris. . . . It would have to be applied over both adrenal glands and possibly also over the cervical and upper thoracic portion of the sympathetic system." According to a personal communication received in 1941 from Professor Schittenhelm, several of his successfully irradiated patients had remained free from relapses for periods of two years.

In this country the disappearance of precordial distress in 5 patients treated for arterial hypertension with combined irradiation of the pituitary and the adrenal glands was mentioned as early as 1935 by Hutton.

Graybiel in a review on "Diseases of the Heart" makes the following comment on the observations of one of us on 100 cases (Raab[b]): "We are frankly skeptical of these results, having used a similar procedure in a small number of cases without success." In a personal letter Dr. Graybiel mentions an improvement in "two or three" patients which "might well have come within the realm of individual variability." Apparently only 400 r and only one single series of treatments had been applied in his patients.

Untoward side-effects were never observed by us or mentioned by any one of the above named investigators, except a lack of appetite or moderate nausea in about 15 per cent of the cases, lasting for only a few days. No signs suggestive of adrenal insufficiency were ever observed. Thus, the warning with which a number of patients were cautioned against the treatment that it is "dangerous" and "likely to produce Addison's disease" appears entirely unfounded.

In none of 7 patients in whom the adrenal hormone level in the blood at rest was determined did it fall below normal limits after roentgen treatment of the adrenal glands (Raab[d]). In 3 irradiated cases (one of them in Europe) who had died, no significant structural changes of the adrenal glands were found at autopsy, except "un-

usually foamy cells" in the cortex of Case 13, more than one year after treatment when he died of cardiac failure. The adrenal cells were "well preserved" in this case.

The essential effect of the treatment seems to consist in the abolition of abnormally intense adrenalin discharges on effort, etc., through suppression of an existing state of abnormal irritability of the nervous mechanism of adrenal medullary secretion. The abnormally intense discharges on physical exercise disappeared in all of 7 patients who were subjected to this test after successful therapeutic irradiation of the adrenal glands (Fig. 3). These observations tend to support the conception of Celotti and Gouin and Bienvenue that moderate roentgen-ray doses applied to the adrenal region exert their functional effects mainly by influencing the supplying nervous sympathetic structures and through "restoration of functional equilibrium."

While the rationale of the treatment in question makes its beneficial effects easily intelligible, it appears more difficult to explain the failure to respond of a substantial percentage of cases. Insufficient dosage alone can hardly be made responsible in a fraction of these: 12 of the 24 unimproved patients of the European series and 2 of our 11 unimproved American patients had received the full dose of three series, or even more, without effect.

Attempts to detect any clinical characteristics of the non-responding patients regarding age, sex, electrocardiogram, past myocardial infarctions and other complicating factors, such as hypertrophic spinal arthritis, were to no avail (Table II). Only a somewhat longer average duration and greater severity of the disease before application of treatment in the non-responding patients seemed to be of a certain, though limited, significance.

The fact that adrenalin is formed not only in the adrenal glands but also by sympathetic nerve fibers in the peripheral vascular system and in the heart muscle itself (Cannon and Lissak) and that stimulation of these nerves increases the myocardial oxygen consumption in the same manner as adrenalin does (Gollwitzer-Meier, Kramer and Krüger) suggests the possibility that a prevalence of this local "adrenergic" mechanism within the heart muscle makes roentgen irradiation of the adrenal glands alone insufficient in certain cases.

The observations of Desjardins and others in regard to a specific depressant effect of roentgen rays upon the irritability of nerve cells may furnish the explanation for the beneficial action of paravertebral and precordial irradiation in angina pectoris as described by Beeck and Hirsch, Morlet, Torbett, Lian, Nemours-Auguste and Barrieu, Gilbert, Arrillaga, Sussman, Samuel and Bowie, Holmes, and Wasch and Schenck.

In our own material paravertebral cervical and thoracic irradiations were added to the adrenal treatments in 4 cases with hypertrophic spinal arthritis. In 2 of these cases this combined form of treatment seemed to improve the results (Cases 9 and 14). The same had been true in 6 of 18 patients treated in Vienna in a similar manner.

The fundamental importance of hormonal cardiometabolic factors in the pathogenesis of angina pectoris is evidenced by a variety of facts: males are very much more afflicted with this disease than females. It becomes apparent, as a rule, at the age of sexual involution. In castrated animals the adrenalin concentration of the heart muscle is increased (Raab[c]), and the latter displays metabolic alterations which are identical with those elicited by adrenalin (Schumann). These changes are normalized through the administration of sex hormones (Schumann). Favorable therapeutic results with sex hormones in angina pectoris were reported by Henssge, Pick, Arndt, Scherf (including normalization of the electrocardiogram), more recently also in this country by Walker, Bonnell, Pritchett and Rardin, Lesser, Hamm, McGavack. Also thyroidectomy has proved to be of therapeutic value in angina pectoris (Lev and Hamburger, Blumgart, Levine and

Berlin, Claiborne and Hurxthal, Clark, Means and Sprague, *et al.*). Since adrenalin was found to accumulate in the heart muscle in maximum concentrations and with maximum speed under the influence of the thyroid hormone (Raab[c]) it seems that the therapeutic effect of thyroidectomy consists essentially in a protection of the heart against the influx of high adrenalin concentrations.

Against the assumed value of roentgen treatment of the adrenal glands for angina pectoris the objection has been raised (von Zimmermann-Meinzingen) that the improvements observed might be of a merely psychic nature. Although such factors may play a rôle in some of the improved patients, it seems difficult to attribute to them a general importance for the following reasons:

(1) It is unlikely that purely imaginary improvements of previously stubbornly intractable anginal attacks should persist uninterrupted for many months and even over periods of years. Only 4 out of 23 improved European patients who were exposed to extreme excitement and fear suffered permanent relapses.

(2) In many cases the improvement was not felt earlier than several weeks after the treatment or after a second or third series. One would expect a purely psychic reaction to take place immediately when the patient is still under the fresh impression of the procedure.

(3) The chemically demonstrable disappearance of the causative abnormal adrenalin discharges during exercise (Fig. 3) and the normalization of exercise electrocardiograms (Raab and Schönbrunner) after the treatments are objective criteria of improvement.

More important seems the possibility of spontaneous improvements and recoveries which are not uncommon in angina cases as pointed out by Levine and White. However, it appears extremely improbable that such spontaneous turns toward the better should have occurred and persisted in 107 out of 142 patients and that they should have coincided with the time of treatments as closely as can be seen from the graphic "complaint curves" (Raab[b]).

Nevertheless it would be highly desirable to have extensive series of both real and sham treatments carried out in medical centers with a large out-patient material and to have the results followed and analyzed in a critical and unbiased manner, not only for practical reasons but also for the purpose of throwing more light upon the problem of the biochemical origin of the angina pectoris syndrome.

It should be re-emphasized in this connection that seemingly non-responding patients who have received less than three series of irradiations within about one year must not be classified as definite failures since one or even two series prove not infrequently an insufficient dose.

The occurrence of a coronary occlusion is to be regarded as a definite contraindication to the treatment for a period of two to three months. An existing state of cardiac decompensation should be controlled with digitalis, and so forth, before treatment is begun. Patients with arterial hypotension or with tuberculosis should not be given roentgen treatment.

SUMMARY

Rationale. Angina pectoris on effort, emotion, and so forth, is believed to be due essentially to the well known acutely anoxiating effect of adrenalin discharges from the adrenal glands upon the heart muscle, the sclerotic coronary arteries of which are unable to dilate adequately and thus to overcome the resulting myocardial anoxia. Clinical and experimental evidence is presented for this theory.

The state of abnormal irritability of the adrenal secretory mechanism which was found to be a characteristic of angina patients could be abolished through roentgen irradiation of the adrenal region without ensuing damage to the basic normal function of the glands. This was demonstrated objectively by quantitative chemical hormone determinations in the blood before

and after treatment and by the normalization of pathological electrocardiograms.

Therapeutic Results. Of 42 typical angina patients treated in Burlington, Vermont, with irradiation of the adrenal region, 74 per cent were either completely freed of their anginal complaints or at least improved for periods ranging between five and forty-five months with an average of two years up to the present.

Nine of the 11 unimproved patients had not received three series of roentgen treatments and thus cannot be considered as definite failures.

No untoward side effects were noted except short episodes of nausea in a few cases.

Death occurred in 7 out of the 42 patients treated during the past four and one-half years.

REFERENCES

Arndt, H. Zur Therapie extragenitaler Störungen mit Sexualhormonen. *Wien. med. Wchnschr.*, 1939, *89*, 222–227.

Arrillaga, F. C. L'angine de poitrine; son traitement par la radiothérapie profonde. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1928, *52*, 949–953.

Barcroft, J., and Dixon, W. E. Gaseous metabolism of mammalian heart. Part 1. *J. Physiol.*, 1906–1907, *35*, 182–204.

Bauer, J. Der Einfluss der Nebennieren und Hypophyse auf die Blutdruckregulation und Umstimmung der Geschlechtscharaktere beim Menschen. *Klin. Wchnschr.*, 1935, *14*, 361–367.

Beeck, L. A., and Hirsch, R. Röntgentiefenstrahlentherapie in der Behandlung von Herz- und Gefässkrankheiten. *Med. Klin.*, 1916, *12*, 877–878.

Blumgart, H. L., Levine, S. A., and Berlin, D. D. Congestive heart failure and angina pectoris; therapeutic effect of thyroidectomy on patients without clinical or pathologic evidence of thyroid toxicity. *Arch. Int. Med.*, 1933, *51*, 866–877.

Bonnell, R. W., Pritchett, C. P., and Rardin, T. E. Treatment of angina pectoris and coronary artery disease with sex hormones. *Ohio State M. J.*, 1941, *37*, 554–556.

Brandt, F., and Katz, G. Ueber den Nachweis von Adrenalinsekretion beim Menschen; die akuten Gefässkrisen. *Ztschr. f. klin. Med.*, 1933, *123*, 40–50.

Brunschwig, A., Humphreys, E., and Roome, N. W. Relief of paroxysmal hypertension by excision of pheochromocytoma. *Surgery*, 1938, *4*, 361–370.

Cannon, W. B. Bodily Changes in Pain, Hunger, Fear and Rage. D. Appleton & Co., New York, 1929.

Cannon, W. B., Aub, J. C., and Binger, C. A. L. Note on effect of nicotine injection on adrenal secretion. *J. Pharmacol. & Exper. Therap.*, 1911–1912, *3*, 379–385.

Cannon, W. B., and Hoskins, R. G. Effect of asphyxia, hyperpnoea and sensory stimulation on adrenal secretion. *Am. J. Physiol.*, 1911–1912, *29*, 274–279.

Cannon, W. B., and Lissak, K. Evidence for adrenaline in adrenergic neurones. *Am. J. Physiol.*, 1939, *125*, 765–777.

Celotti, A. Ricerche istologiche sul comportamento delle surrenali e in particolar modo della loro innervazione di fronte all'azione dei raggi X. *Boll. Soc. Ital. di biol. sper.*, 1931, *6*, 998–100.

Claiborne, T. S., and Hurxthal, L. M. Results of total thyroidectomy in heart disease. *New England J. Med.*, 1937, *216*, 411–417.

Clark, R. J., Means, J. H., and Sprague, H. B. Total thyroidectomy for heart disease. *New England J. Med.*, 1936, *214*, 277–294.

Cottenot, P. H. Action des rayons X sur les glandes surrénales. Thèse de Paris, 1913.

Cottrell, J. E., and Wood, F. C. Effect of epinephrin in angina pectoris. *Am. J. M. Sc.*, 1931, *181*, 36–39.

von Decastello, A. Ueber Veränderungen an der Nebennieren nach Röntgenbestrahlung. *Wien. klin. Wchnschr.*, 1912, *25*, 759.

Deneke, T. Tabak und Angina pectoris. *Ztschr. f. ärztl. Fortbild.*, 1936, *33*, 573–576.

Desjardins, A. U. Analgesic property of roentgen rays. *Radiology*, 1927, *8*, 317–324.

Desjardins, A. U. Effect of irradiation on suprarenal gland. Am. J. Roentgenol. & Rad. Therapy, 1928, *19*, 453–461.

Eichholtz, F. Ueber den Einfluss von Nikotin und nikotinartig Wirkenden Substanzen auf die Adrenalinsekretion. *Arch. f. exper. Path. u. Pharmakol.*, 1923, *99*, 172–184.

Engelstad, R. B., and Torgersen, O. Experimental investigations on effects of roentgen rays on suprarenal glands in rabbits. *Acta radiol.*, 1937, *18*, 671–687.

Evans, C. L., and Ogawa, S. Effect of adrenalin on gaseous metabolism of isolated mammalian heart. *J. Physiol.*, 1914, *47*, 446–459.

Frey, H. Experimentelle Untersuchungen über die Röntgensensibilität der Nebennieren. *Acta radiol.*, 1928, *9*, 23–53.

Gilbert, R. Ueber die Röntgentherapie der Angina pectoris. *Strahlentherapie*, 1936, *57*, 203–223.

Gollwitzer-Meier, K., Kramer, K., and Krüger, E. Die Wirkung des Adrenalins auf die Energetik des Herzens. *Arch. f. d. ges. Physiol.*, 1936, *237*, 639–650.

Gouin, J., and Bienvenue, A. Transmission par injection de sang, de caractères sanguines acquis par la radiothérapie sympathique. *Bull. et mém. Soc. de radiol. méd. de France*, 1929, *17*, 286–288.

Grabfield, G. P., and Squier, T. L. Note on effect of irradiation of the suprarenal region in rabbits with Roentgen rays. *Arch. Int. Med.*, 1921, *27*, 168–174.

Graybiel, A. Diseases of the heart; review of significant contributions made during 1940. *Arch. Int. Med.*, 1941, *67*, 1061–1092.

Green, H. D., Wegria, R., and Boyer, N. H. Effects of epinephrine and pitressin on the coronary artery inflow in anesthetized dogs. *J. Pharmacol. & Exper. Therap.*, 1942, *76*, 378–391.

Gremels, H. Ueber die Steuerung der energetischen Vorgänge am Säugetierherzen. *Arch. f. exper. Path. u. Pharmakol.*, 1936, *182*, 1–54.

Hadorn, W. Untersuchungen des Herzens im hypoglykämischen Schock. *Arch. f. Kreislaufforsch.*, 1937, *2*, 70–156.

Hamm, L. Testosterone propionate in the treatment of angina pectoris. *J. Clin. Endocrinol.*, 1942, *2*, 325–328.

Harvey, W. G. On the pathological effects of Roentgen rays on animal tissues. *J. Path. & Bacteriol.*, 1907–1908, *12*, 549–556.

Henssge, E. Die Beseitigung vasomotorischer Störungen durch Testoviron und eine vergleichende Darstellung über die Wirkung männlicher Hormone. *Aerztl. Korrespondenz*, 1937, *21*, 537.

Holfelder, H., and Peiper, H. Die Strahlenempfindlichkeit der Nebennieren und Wege zur Verhütung von Nebennierenschädigungen in der Röntgentiefentherapie. *Strahlentherapie*, 1923, *15*, 1–17.

Holmes, G. W. Discussion by paper by Samuel and Bowie.

Hutton, J. H. Radiotherapeutic treatment of hypertension and diabetes. *Radiology*, 1935, *24*, 330–341.

Katz, L. N., Hamburger, W. W., and Lev, M. Diagnostic value of epinephrine in angina pectoris. *Am. Heart J.*, 1932, *7*, 371–379.

Keefer, C. S., and Resnik, W. H. Angina pectoris; syndrome caused by anoxemia of myocardium. *Arch. Int. Med.*, 1928, *41*, 769–807.

Kobro, M. S. Nicotinwirkung und Adrenalinsekretion. Johan Grundt-Tanum, Oslo, 1936.

Kugelmann, B. Zur Frage der Adrenalinausschüttung bei der Insulinhypoglykämie und bei Palschen Gefässkrisen. *Klin. Wchnschr.*, 1933, *12*, 1488–1489.

Külbs, F. Zur Symptomatologie des Tabakrauchens. *Ztschr. f. klin. Med.*, 1924, *99*, 258–263.

La Barre, J., and Houssa, P. A propos des variations de l'adrénalinémie au cours de l'hypoglycémie insulinique. *Compt. rend. Soc. de biol.*, 1932, *109*, 967–969.

Lenhartz, H. Ueber paroxysmale Blutdrucksteigerungen. *Klin. Wchnschr.*, 1939, *18*, 109.

Lepeschkin, E. W. Ueber das Elektrokardiogramm bei experimenteller Koronarinsuffizienz. *Cardiologia*, 1938, *2*, 236–272.

Lesser, M. A. Treatment of angina pectoris with testosterone propionate. *New England J. Med.*, 1942, *226*, 51–54; 1943, *228*, 185–188.

Lev, M. W., and Hamburger, W. W. Studies in thyroid heart disease; angina pectoris and hyperthyroidism. *Am. Heart J.*, 1932, *8*, 109–113.

Levine, H. B., and White, P. D. What sensible living and natural recovery can do for a cardiac patient. *New England J. Med.*, 1941, *225*, 101–105.

Levine, S. A., Ernstene, A. C., and Jacobson, B. M. Use of epinephrine as diagnostic test for angina pectoris. *Arch. Int. Med.*, 1930, *45*, 191–200.

Levy, R. L., Williams, N. E., Bruenn, H. G., and Carr, H. A. The "anoxemia test" in diagnosis of coronary insufficiency. *Am. Heart J.*, 1941, *21*, 634–656.

Lian, C., Barrieu, R., and Nemours-Auguste. Technique et résultats de la radiothérapie dans l'angine de poitrine. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1928, *52*, 1030–1041.

Lippross, O. Zur Pathologie und Therapie der Angina pectoris. *München. med. Wchnschr.*, 1940, *87*, 727–730.

Martin, C. L., Rogers, F. T., and Fisher, N. F. Effect of roentgen rays on adrenal gland. Am. J. Roentgenol. & Rad. Therapy, 1924, *12*, 466–471.

McGavack, T. H. Angina-like pain: a manifestation of male climacterium. *J. Clin. Endocrinol.*, 1943, *3*, 71–80.

Morlet, Radiothérapie dans les affections du système cardio-vasculaire. *Ann. de méd. phys.*, 1922, *16*, 212–221.

Nuzum, F. R., and Dalton, J. W. Paroxysmal and persistent hypertension in association with lesions of adrenal glands. *Am. Heart J.*, 1938, *16*, 643–662.

Pick, R. Die hormonale Behandlung der Keimdrüseninsuffizienz beim Manne mit Berücksichtigung des synthetischen Testosteron-propionats Perandren. *Med. Klin.*, 1938, *34*, 17–19.

a Raab, W. Angina pectoris simplex und hämodynamische Herzbelastung. *Ztschr. f. klin. Med.*, 1938, *134*, 595–603.

b Raab, W. Roentgen treatment of adrenal glands in angina pectoris (100 cases). *Ann. Int. Med.*, 1940, *14*, 688–710.

c Raab, W. Chemical determinations of adreno-cortical (AC) hormones in heart muscle of the rat. *Endocrinology*, 1941, *29*, 564–573.

d Raab, W. Abnormal suprarenal discharges in angina pectoris and their control by x-ray therapy. *J. Clin. Endocrinol.*, 1941, *1*, 977–982.

e Raab, W. Unpublished data.

f Raab, W. Blood level of adrenalin and related substances in various experimental and clinical conditions. *Exper. Med. & Surg.*, 1943, *1*, 402–412.

g Raab, W. Adrenalin and related substances in blood and tissues. *Biochem. J.*, 1943, *37*, 470–473.

Raab, W., and Schönbrunner, E. Die Normalisierungstendenz des Elektrokardiogrammes nebennierenbestrahlter Angina pectoris-Kranker. *Arch. f. Kreislaufforsch.*, 1939, *4*, 362–386.

Raab, W., and Soule, A. B. Effect of roentgen irradiation on the hormone content and secretion of the adrenal medulla. *Radiology*, 1943, *41*, 56–60.

Rein, H. Ueber die physiologischen Aufgaben des Adrenalins als Kreislaufhormon. *Verhandl. d. deutsch. Gesellsch. f. Kreislaufforsch.*, 1937, pp. 27–58.

Rothschild, M. A., and Kissin, M. Production of anginal syndrome by induced general anoxemia. *Am. Heart J.*, 1933, *8*, 729–744.

Samuel, E. C., and Bowie, E. R. Therapeutic application of roentgen ray in angina pectoris. Am. J. Roentgenol. & Rad. Therapy, 1932, *27*, 870–876.

Scherf, D. Ueber das Elektrokardiogramm bei Störungen der Ovarialtätigkeit. *Klin. Wchnschr.*, 1938, *17*, 44–47.

Schittenhelm, A. Aus dem Indikationsgebiet der Strahlenbehandlung von Hypophyse, Schilddrüse und Nebenniere. *Strahlentherapie*, 1939, *66*, 373–427.

Schönbrunner, E. Ueber einen Fall von Schädigung des Herzmuskels durch Insulin. *Med. Klin.*, 1935, *31*, 1571–1572.

Schumann, H. Der Einfluss der männlichen Sexualhormone auf den Glykogen-, Phosphagen- und Adenylpyrophosphatgehalt des Herzmuskels. *Klin. Wchnschr.*, 1939, *18*, 925–927.

Shambaugh, P., and Cutler, E. C. Total thyroidectomy in angina pectoris; experimental study. *Am. Heart J.*, 1934, *10*, 221–229.

Stewart, G. N., and Rogoff, J. M. Action of drugs on output of epinephrin from the adrenals. III. Nicotine. *J. Pharmacol. & Exper. Therap.*, 1919–1920, *13*, 183–241.

Strauss, L. H. Nikotinwirkungen und -schädigungen. *Ergebn. d. inn. Med. u. Kinderh.*, 1937, *52*, 375–438.

Sussman, M. L. Treatment of angina pectoris by paravertebral short wave radiation. Am. J. Roentgenol. & Rad. Therapy, 1930, *24*, 163–168.

Torbett, J. W. X-ray treatment of angina pectoris and peribronchial adenopathy. *Am. J. Phys. Therapy*, 1929, *6*, 272.

Tsuzuki, M. Experimental studies on biological action of hard roentgen rays. Am. J. Roentgenol. & Rad. Therapy, 1926, *16*, 134–150.

Vesa, A. Untersuchungen über die Einwirkung des Adrenalins auf das Elektrokardiogramm. *Acta Soc. med. fenn. duodecim* (Ser. B, fasc. 3, art. 10), 1939, *26*, 1–49.

Walker, T. C. Use of testosterone propionate and estrogenic substance in cardiovascular disease. *Med. Rec. & Ann.*, 1940, *34*, 667.

Wasch, M. G., and Schenck, S. G. Roentgen therapy in angina pectoris; report of sixty-five cases. Am. J. Roentgenol. & Rad. Therapy, 1938, *39*, 585–589.

Wenckebach, K. F. Herz- und Kreislaufinsuffizienz. Second edition. Theodor Steinkopff, Dresden, 1932.

von Zimmermann-Meinzingen, O. Ueber Angina pectoris. *Wien. klin. Wchnschr.*, 1938, *51*, 1301–1304.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Editor: LAWRENCE REYNOLDS, M.D. *Assistant Editor:* RUTH BIGELOW, B.S.

Editorial Board: A. C. CHRISTIE, M.D. E. H. SKINNER, M.D. LAURISTON S. TAYLOR
Advisory Board for Pathology: EUGENE L. OPIE, M.D.
Collaborating Editors: The Officers and Committee Members of the Societies of which this JOURNAL is the official organ, whose names appear on this page, are considered collaborating editors of this JOURNAL. *Foreign Collaborators:* GÖSTA FORSSELL, M.D., STOCKHOLM, G. F. HAENISCH, M.D., HAMBURG, R. LEDOUX-LEBARD, M.D., PARIS.

Publisher: CHARLES C THOMAS, 220 East Monroe Street, Springfield, Illinois.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich., Office of publication, 220 E. Monroe Street, Springfield, Ill. Information of interest to all readers will be found on page iv.

Officers and Standing Committees

AMERICAN ROENTGEN RAY SOCIETY

President, Sherwood Moore, St. Louis, Mo.; *President-Elect,* Lyell C. Kinney, San Diego, Calif.; *1st Vice-President:* P. C. Hodges, Chicago, Ill. *2nd Vice-President:* Aubrey O. Hampton, Boston, Mass.; *Secretary:* H. Dabney Kerr, University Hospital, Iowa City, Iowa; *Treasurer:* J. B. Edwards, 144 Woodridge Place, Leonia, N. J. *Historian:* Ramsay Spillman, New York, N. Y.

Executive Council: Sherwood Moore, L. C. Kinney, P. C. Hodges, A. O. Hampton, H. D. Kerr, J. B. Edwards, Lawrence Reynolds, F. B. Bogart, V. W. Archer, U. V. Portmann, W. M. Doughty, R. S. Bromer, C. M. Richards, J. C. Dickinson, Charles H. Heacock, Chairman, 915 Madison Ave., Memphis, Tennessee.

Program Committee: C. H. Heacock, Memphis, Tenn., H. D. Kerr, Iowa City, Iowa, Lawrence Reynolds, Detroit, Mich., V. W. Archer, University, Va., U. V. Portmann, Cleveland, Ohio, Lyell C. Kinney, Chairman, 1831 Fourth St., San Diego, Calif.

Publication Committee: E. P. Pendergrass, Philadelphia, Pa., J. T. Case, Chicago, Ill., U. V. Portmann, Chairman, Cleveland, Ohio.

Finance Committee: J. C. Peden, St. Louis, Mo., E. L. Jenkinson, Chicago, Ill., F. B. Bogart, Chairman, Chattanooga, Tenn.

Committee on Scientific Exhibits: P. A. Bishop, Philadelphia, Pa., S. W. Donaldson, Ann Arbor, Mich., V. W. Archer, Chairman, University, Va.

Representative on National Research Council: Karl Kornblum, Philadelphia, Pa.

Editor: Lawrence Reynolds, 110 Professional Building, Detroit 1, Mich.

Assistant Editor: Ruth Bigelow, 110 Professional Building, Detroit 1, Mich.

Editorial Board: A. C. Christie, E. H. Skinner, Lauriston S. Taylor.

Advisory Board for Pathology: Eugene L. Opie.

Forty-fifth Annual Meeting: Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Palmer House, Chicago, Ill., Sept. 24–29, 1944.

AMERICAN RADIUM SOCIETY

President: William E. Costolow, Los Angeles, Calif.; *President-Elect:* Charles L. Martin, Dallas, Texas; *1st Vice-President:* Frank E. Adair, New York, N. Y.; *2nd Vice-President:* Eugene P. Pendergrass, Philadelphia, Pa.; *Secretary:* A. N. Arneson, 4952 Maryland Ave., St. Louis, Mo. (*Acting Secretary,* E. H. Skinner, 1532 Professional Bldg., Kansas City, Mo.); *Treasurer:* Leland R. Cowan, 606 Medical Arts Bldg., Salt Lake City, Utah.

Executive Committee: Lawrence A. Pomeroy, Chairman, Cleveland, Ohio, Frederick W. O'Brien, Boston, Mass., Hayes E. Martin, New York, N. Y.

Program Committee: Charles L. Martin, Chairman, Dallas, Texas, William S. MacComb, New York, N. Y., Eugene T. Leddy, Rochester, Minn., Herbert E. Schmitz, Chicago, Ill., John S. Bouslog, Denver, Colo.

Publication Committee: E. H. Skinner, Chairman, Kansas City, Mo., Zoe A. Johnston, Pittsburgh, Pa., Wilbur Bailey, Los Angeles, Calif.

Research and Standardization Committee: Edith H. Quimby, Chairman, New York, N. Y., J. L. Weatherwax, Philadelphia, Pa., W. S. MacComb, New York, N. Y.

Education and Publicity Committee: Ernst A. Pohle, Chairman, Madison, Wis., William H. Sargent, Oakland, Calif., Robert B. Taft, Charleston, S. C.

Janeway Lecture Committee: Douglas Quick, Chairman, New York, N. Y., E. H. Skinner, Kansas City, Mo., G. Failla, New York, N. Y., L. A. Pomeroy, Cleveland, Ohio, F. W. O'Brien, Boston, Mass., H E. Martin, New York, N. Y.

Representatives on American Board of Radiology: Douglas Quick, New York, N. Y., B. P. Widmann, Philadelphia, Pa., F. W. O'Brien, Boston, Mass.

Twenty-eighth Annual Meeting: 1944, to be announced.

EDITORIAL

EFFECT OF ROENTGEN THERAPY ON THE HEART

IN 1932, Desjardins[1] made an exhaustive review of the medical literature dealing with the action of roentgen and radium rays on various organs of the body. He found all the evidence available at that time pointing to the fact that the specific radiosensitivity of the heart is definitely less in comparison with that of most of the other organs and that ordinary therapeutic doses of radiation exert no injurious effect on it. In particular, the animal experiments indicated that, to produce direct degenerative changes of the heart muscle, extremely high doses, surpassing many times those of clinical practicability, were necessary. Changes were at times obtained from smaller doses but they were thought to be secondary to inflammatory reaction induced in the lungs which are considerably more susceptible to irradiation damage than the heart or to represent the effect of the circulation through the organ of toxic products from more generalized irradiation and accompanying disturbances of nutrition. In young animals (embryos) a retarding growth effect of the rapidly developing heart was noted. However, this, too, was explained on the basis of general inhibition of growth of the organism as a whole rather than a specific action of the irradiation on the heart itself.

The animal experiments as well as clinical observations further indicated that irradiation, either by the use of roentgen rays or radium, does not have a direct effect on the blood pressure, although a fall may result indirectly from a general systemic reaction or certain depressive effects on the vasomotor centers.

Since Desjardins' publication, there have been few additional contributions to the literature. It appears that the conclusions reached represented the final answer to the problem and that nothing worth while could be gained from continuation of the investigations.

During the last few years, however, the ever increasing popularity of the fractionated protracted method of irradiation with very large cumulative doses and the gradual extension of high voltage roentgen therapy to the supervoltage and megavoltage fields have created new clinical situations which make the opening of the subject very desirable both from the experimental and the clinical standpoint. It is fortunate, therefore, that Leach and his coworkers have undertaken the first step in this direction and that in several subsequent publications, the series of which is not yet complete, they have brought to light valuable new information which cannot fail to enrich the clinical knowledge of the radiotherapist.

The initial publications of the series deal with animal experiments. This study was made with the purpose of determining the immediate and late effect of roentgen rays on the heart of laboratory animals. As indicated in the series of Desjardins, there have been several authors who have investigated the immediate effect, but there is apparently only one published record, that of Domagk[2] on the late effect. On the other hand, clinical experience shows that in other structures or organs, such as skin, subcutaneous tissue, muscle, bone, and so forth, late damage often results when the immediate effect following the irradiation

[1] Desjardins, A. U. Action of roentgen rays and radium on the heart and lungs. Am. J. Roentgenol. & Rad. Therapy, 1932, *27*, 149; 303; 477.

[2] Domagk, G. Gewebsveränderungen nach Röntgenbestrahlungen. *Ergebn. d. inn. Med. u. Kinderh.*, 1928, *33*, 1–62.

was what, with our present methods of analysis, we would consider to be within normal limits. The question arose whether or not the heart would exhibit a similar behavior.

To answer this question, Leach and Sugiura[3] in a first series of experiments accurately established the physical magnitude of the dose, expressed in roentgens, that can be administered to the heart of rats to produce a recordable immediate effect. They used roentgen rays obtained with 200 kv., 0.5 mm. Cu, and irradiated the heart through a precordial window 1 by 1.5 cm. in size, the entire animal being covered by lead. Since the fractionated protracted method of irradiation would be most difficult to carry out, large single doses of 1,500, 3,000, 5,000, 7,500, 10,000, and 20,000 r were given. The results of these experiments supported the conclusions of previous investigators that the heart is extremely radioresistant. The critical dose for the myocardium was found to be 10,000 r or more, when capillary hemorrhage, round cell infiltration, myocardial degeneration and necrosis followed. The pericardium and endocardium withstood doses up to and including 20,000 r.

In their second series of animal experiments, Leach and Sugiura[4] extended the period of observation to from two to fourteen months after irradiation to determine if any late changes, particularly fibrosis, could be detected. Domagk[2] in his experiments found that fatty degeneration and necrosis was followed, after a time, by the interstitial proliferation of fibroblasts and therefore it was important to clarify this point. The irradiation was carried out with a technique identical with that of the first series and the doses were of the same magnitude. The results revealed that there was no demonstrable effect on the heart of rats using single doses up to and including 7,500 r. As already stated, 10,000 r represents the critical dose for the myocardium. If one could get a sufficient number of animals to survive such doses, it is likely that the immediate effect would give place to fibrosis of the myocardium, thus supporting the observations of Domagk.

In extending these experiments, Leach and Sugiura further found that no late changes in the heart of rats could be demonstrated when the roentgen rays were administered over the lungs or thigh muscle and that pulmonary infection, when present, likewise remained without effect on the heart. To explain the extremely high radioresistance of the heart, as compared to other structures of the body, Leach and Sugiura accept the fluid flow theory of Failla.[5] They believe that it is compatible with this theory to assume that the myocardium can cope with the increased ionic concentration produced by the roentgen rays up to 7,500 r but above that the intracellular concentration becomes too high to be consistent with normal metabolism of cell life.

In coordinating the above experimental data with clinical facts, Leach and his associates made some interesting new observations. A systematic study of several groups of patients since 1938 revealed in numerous instances definite disturbances of the heart and circulation following roentgen therapy for the treatment of cancer of different regions of the body. At first glance, this appeared to contradict the experimental results and therefore investigations in other directions were in order. Leach, Farrow, Foote and Wawro[6] made an exhaustive study of the fibrosis of the lung occurring following roentgen irradiation for cancer of the breast. Soon afterward, Leach[7] published his novel interpretation of the pulmonary physiology in chronic irradiation

[3] Leach, J. E., and Sugiura, K. Effect of high voltage roentgen rays on the heart of adult rats. AM. J. ROENTGENOL. & RAD. THERAPY, 1941, *45*, 414–425.

[4] Leach, J. E., and Sugiura, K. Late effect of high voltage roentgen rays on the heart of adult rats. AM. J. ROENTGENOL. & RAD. THERAPY, 1942, *48*, 81–87.

[5] Failla, G. Theory of biological action of ionizing radiations. *Cancer Probl., Symposium*, 1937, pp. 202–214.

[6] Leach, J. E., Farrow, J. H., Foote, F. W., Jr., and Wawro, N. W. Fibrosis of the lung following roentgen irradiation for cancer of the breast. AM. J. ROENTGENOL. & RAD. THERAPY, 1942, *47*, 740–747.

[7] Leach, J. E. Abnormal pulmonary physiology as a result of chronic irradiation pleuropulmonitis. AM. J. ROENTGENOL. & RAD. THERAPY, 1943, *50*, 772–778.

pleuropulmonitis, according to which the abnormal function of the thoracic wall, mediastinum and diaphragm is almost as important in causing the pulmonary dysfunction as the pleuropulmonary fibrosis itself. Furthermore, there is evidence accumulating that the cause of the pericarditis and adhesions between the pericardium and pleura in such instances is not a primary roentgen effect, but extension of an inflammatory reaction to those membranes from the contiguous lung. These observations are important as we shall see from the point of view of correct electrocardiographic interpretations.

In two very recent papers,[8,9] Leach finally presented the results of his painstaking clinical observations on the effect of the roentgen rays on the heart of humans. For this study 85 patients were chosen and in order to obtain comparable data they were placed in three groups. Group I included those with cancer of the head, neck, female genital tract and rectum, in which no radiation therapy was delivered to the thorax. Group II included those with malignant lymphoma or teratoma in which the irradiation was rather general, always extending to the thorax. Group III included those with cancer of the breast, lung, esophagus and cardiac end of the stomach, in which roentgen therapy was confined to the thorax alone. Apart from the routine examinations made in conjunction with the cancer, the study consisted of (1) history with particular reference to the cardiovascular system, (2) a physical examination, (3) roentgenoscopic and teleroentgen examination of the chest and heart and (4) electrocardiographic examination. All examinations were made prior to roentgen therapy and at various intervals thereafter, depending on the individual findings. The follow-up period ranged from a few months, in those who died or became lost to other institutions, to over three years.

A careful analysis of all cases of the three groups revealed that there was no evidence that roentgen therapy *per se* caused injury to the heart or that it was responsible for the complications that arose. In Group III, three patients were observed who developed chronic pericarditis or pleuropericardial adhesions following heavy roentgen therapy over the chest. However, since according to the animal experiments, the pericardium can resist even larger doses of roentgen rays than the myocardium, it is probable that the changes were secondary to the chronic infection of the thoracic wall, ribs and left lung which was present in all three instances. As the infection progressed, the pericardium became invaded because of its contiguity.

Independent from the series mentioned above, Leach also observed four cases of carotid sinus syndrome occurring during the course of roentgen therapy. These cases had metastatic carcinoma of the upper cervical lymph nodes intimately associated with the carotid bifurcation plus considerable secondary infection. The episodes consisted of sudden syncope, slow pulse, lowered blood pressure and in two cases brief epileptiform seizures which were promptly relieved by atropine or ephedrine sulfate. Following completion of the irradiation and clearing up of the infection, the episodes completely and permanently ceased. In several cases of the series, a depression of the blood pressure was noted but this was thought to be more likely due to insufficient nourishment, anemia, fever, neoplastic toxemia and only to a lesser extent to a general irradiation effect. Contrary to other observers, the author found cardiac arrhythmia developing only infrequently as a result of roentgen therapy. Whenever it occurred, it could easily be traced to some other cause.

The most outstanding findings—the ones which in fact could create a great deal of confusion—were in connection with the electrocardiographic examinations. In general, two types of variations from the normal were noted. The first occurred in pa-

[8] Leach, J. E. Some of the effects of roentgen irradiation on the cardiovascular system. Am. J. Roentgenol. & Rad. Therapy, 1943, *50*, 616–628.

[9] Leach, J. E. Effect of roentgen therapy on the heart. *Arch. Int. Med.*, 1943, *72*, 715–745.

tients of all the groups, quite irrespective of whether or not heart disease was present prior to the roentgen treatment. It consisted in a minor variation of all the waves, reflecting a change in the physiologic state of the myocardium. The cause may be attributed to anemia, infection, cachexia, toxemia and perhaps a depressing effect of the roentgen irradiation itself. The second alteration occurred only in patients who had radiation therapy over the thorax. It was limited to the ventricular complex and while there were frequent unpredictable changes in the voltages of the QRS waves, the variation in the configuration of the T wave seemed to follow a definite pattern. When there was an appreciable degree of irradiation pleuropneumonitis with attendant mediastinal shift and elevation of the diaphragm in the left hemithorax, the T wave in lead I became progressively lowered and even negative, while its reciprocal, T_3, became higher. Conversely, when the above changes occurred in the right hemithorax, T_1 became higher and T_3 lower, although the variations were never as marked as on the left side. Finally, when the mediastinum received the bulk of the irradiation, the alteration was the least marked, consisting of only minor variations of the voltages of the different waves. The configuration of an electrocardiogram depends, among other things, on the direction of the pathways conducting the action current from the epicardial surface of the heart to the extremities. Leach therefore assumes that the above T wave changes may well be explained on the basis of the altered relation of the heart to the thoracic wall, the elevated diaphragm and the posterior muscle mass through which the bulk of the action current is carried away from the heart. For the same reason, the alteration of the T wave appeared greatest when the irradiation was made on the left side, less marked when the irradiation was made on the right side and practically undisturbed when the irradiation was made over the mediastinum. That these electrocardiographic changes cannot be caused by injury to the heart itself Leach seems quite certain.

Obviously, it will remain for the future to furnish additional data on this very important subject. For the present, we can safely make the premise that no damage is being done to the heart itself by the various methods of irradiation as currently used in clinical roentgen therapy. The observations should be extended, however, to cover the entire life span of the treated individual and they should also include the higher ranges of supervoltage and megavoltage roentgen therapy.

T. Leucutia

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Joint Meeting of American Roentgen Ray Society and Radiological Society of North America, Palmer House, Chicago, Ill., Sept. 24–29, 1944.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Chicago, Ill., June 12–16, 1944.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Joint Meeting of American Roentgen Ray Society and Radiological Society of North America, Palmer House, Chicago, Ill., Sept. 24–29, 1944.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. Earl R. Miller, University of California Hospital, San Francisco, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. D. D. Brannan, 11311 Shaker Blvd., Cleveland 4, Ohio. Meets at 6:30 P.M. at Allerton Hotel on fourth Monday each month, October to April, inclusive.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

Denver Radiological Club
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Acting Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport. Annual meeting at Penn Alto Hotel, Altoona, Pa., May 13–14, 1944.

Philadelphia Roentgen Ray Society
Secretary, Dr. R. P. Barden, University Hospital, Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. P. C. Schnoebelen, 462 N. Taylor Ave. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Diego Roentgen Society
Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

San Francisco Radiological Society
Secretary, Dr. Martha Mottram, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months of year at Toland Hall, University of California Hospital, second six months at Lane Hall, Stanford University Hospital.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. Herman Klapproth, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton, Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Announcing . . .

A JOINT MEETING

of

THE AMERICAN ROENTGEN RAY SOCIETY

and

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

at

THE PALMER HOUSE, CHICAGO, ILLINOIS

SEPTEMBER 24 TO 29, 1944

The officers and members of the Program Committees of the American Roentgen Ray Society and the Radiological Society of North America, at a meeting held in Chicago, February 12, 1944, decided that the interests of all radiologists on the North American continent could best be served by conducting a joint meeting in 1944.

It appears obvious that, by having such a meeting, radiologists in military and civilian practice could obtain much valuable information regarding the recent technical and scientific advances in radiology. The dissemination of such knowledge is recognized as a valuable contribution to the successful prosecution of our military activities.

Because of its central location, Chicago was selected as the most desirable city for such a meeting. Prompt action was necessary in order to obtain adequate hotel facilities, and we have been assured that sufficient rooms will be made available at the Palmer House for those who wish to attend.

It is not too early to make your plans for the meeting, and you are invited to submit contributions for the scientific program and exhibits as soon as possible.

LYELL C. KINNEY, *President-Elect*
American Roentgen Ray Society

ELDWIN R. WITWER, *President*
Radiological Society of North America

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

A RADIOPAQUE LIQUID LATEX INJECTION MEDIUM FOR BLOOD VESSELS

By C. E. TOBIN
Department of Anatomy, The University of Rochester School of Medicine and Dentistry
ROCHESTER, NEW YORK

A postmortem study of main or collateral blood vessels is desired frequently in conditions where disease or surgical intervention have occluded parts of the vascular system. In such studies, an injection medium which possesses radiopaque properties, in addition to filling the desired vessels with a pigmented rubber-like medium, would be the ideal solution whereby the course of the vessels involved could be determined by roentgenograms and by subsequent dissection.

Pigmented liquid latex, an aqueous, colloidal, rubber solution, has been found to be an ideal injection medium for dissection of blood vessels in laboratory specimens because of its ability to: (1) be colored with fast, soluble dyes; (2) penetrate into the smallest vessels without staining adjacent tissue; (3) be used cold and be diluted to the desired consistency by addition of distilled H_2O; (4) set into a tough, flexible cast of vessels (where not deposited in too large masses) by reacting with phenol, phenolic compounds, formalin or acids.[1] A syringe with a glass cylinder and rubber piston should be used for injection, as latex will cause the plunger of "all glass" or "all metal" syringes to adhere to the cylinder walls.

Pigmented latex alone has very little radiopacity even when "soft tissue technique" is used. The following experiments were tried, therefore, to find a suitable radiopaque medium which could be mixed with pigmented latex and still retain the qualities of latex listed above.

Samples of red liquid latex (pH 9.9) were mixed with sodium iodomethane sulfonate (skiodan), crystalline potassium iodide, barium sulfate, tetraiodophenolphthalein sodium salt (tetradol emulsion), and ethyl iodophenylundecylate (pantopaque) and tested by injection into rats.* Each of the first four substances when added directly to the stock solution of latex coagulated it, making these combinations unsuitable for injection. However, a small quantity of these substances could be added to the latex, but the amount was insufficient to produce a continuous roentgenographic shadow in the injected animals, even though the mixture remained fluid for injection at pH 10 (Fig. 1). Pantopaque, on the other hand, was found to form a stable emulsion with latex, but 50 per cent or more of this substance had to be mixed with the latex for good contrast (Fig. 2 and 3). Pantopaque, being an oily medium, caused an increase in the viscosity of the latex-pantopaque mixture, which could be overcome partly by raising the pH to 10.78 with the addition of NH_4OH. The arteries of the material studied were injected as soon as possible after death with pantopaque-latex mixture, the specimens roentgenographed after injection, and later preserved either with our stock of embalming solution (pH 2.6) or with a

[1] Gamble, D. L. Liquid latex as an injection mass for blood-vessels. *Science*, 1939, 90, 520.

* The radiopaque media were furnished by the Department of Radiology, University of Rochester School of Medicine and Dentistry.

formalin-acetic acid mixture (pH 3.3). Several days later when the latex had hardened, the specimens were dissected to confirm the extent of the injection.

The clinical value of this injection medium, in studying the vascular system, is demonstrated by the following case, which will be presented more in detail as a separate report from the Department of Surgery, The University of Rochester School of Medicine and Dentistry.

J. G., white male, aged fifty-two. Dissecting

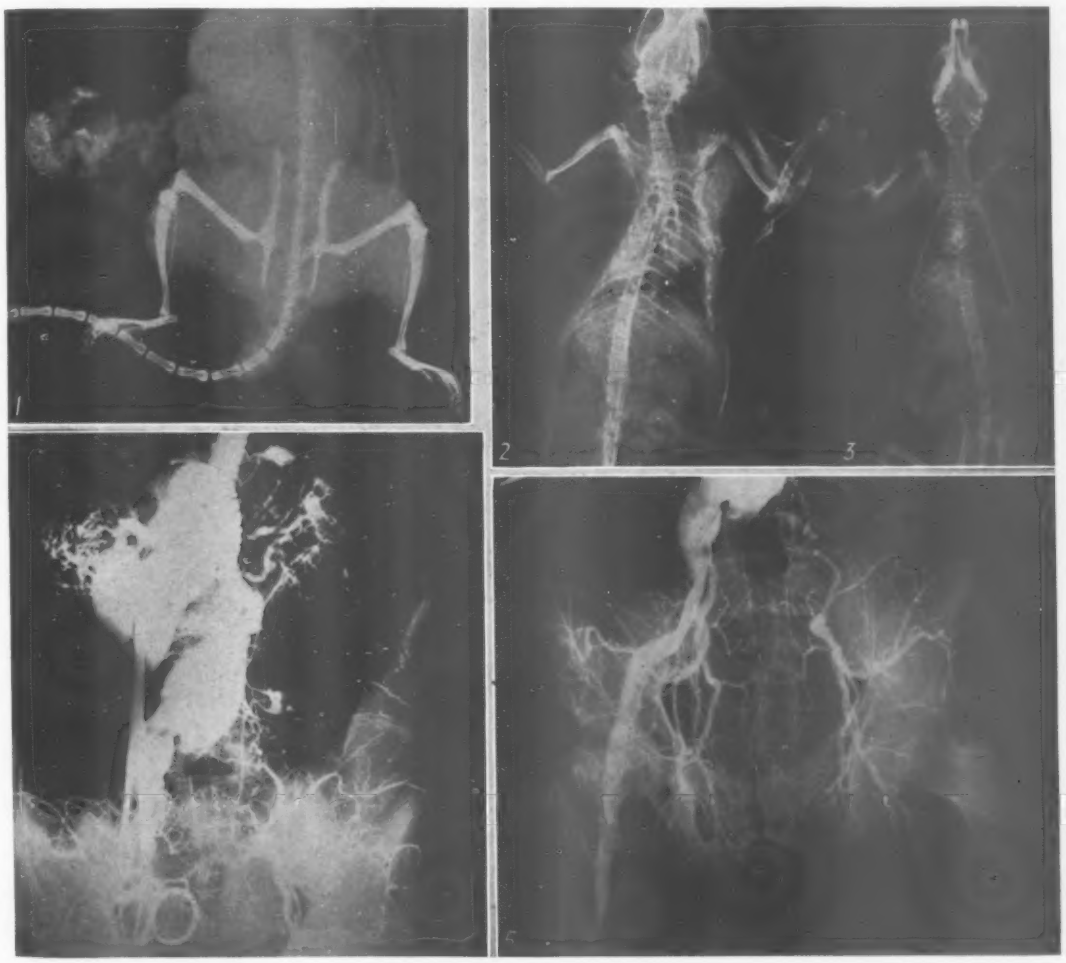


Fig. 1. Discontinuous shadow made by a saturated solution of potassium iodide-latex in the viscera of a rat. Similar shadows were made by a saturated solution of barium, skiodan and tetradol emulsion when mixed with latex. The arteries of this and the other experimental animals were filled with the injection medium.

Fig. 2. A continuous outline of the right carotid artery of a rat was seen after injection with 50 per cent pantopaque-latex.

Fig. 3. A 20 per cent pantopaque-latex mixture was insufficient to produce a distinct shadow.

Fig. 4. Roentgenogram of case reported showing shadows from the main and smaller arteries as well as the aortic and right iliac aneurysm, and portion of the jejunum (at tip of clamp) filled with injection medium.

Fig. 5. Roentgenogram of case reported showing aneurysm of aorta and right iliac artery, as well as all the branches of the right iliac and hypogastric artery, filled with the contrast medium. The left iliac artery is obliterated but branches of the lumbar and sacral arteries formed anastomotic channels with the left hypogastric. The branches of the latter artery, although enlarged, were patent and normal in their distribution to the gluteal region and left stump. No enlargement of the hemorrhoidal vessels is seen.

aneurysm and thrombosis of left common iliac artery in addition to aneurysmal dilatation both of aorta, proximal to its bifurcation, and of proximal part of right iliac artery, were ascertained by laparotomy on January 25, 1942. The aorta was occluded by two tape ligatures between the origin of the inferior mesenteric artery and the aortic aneurysm, January 29. The left extremity was amputated at mid-thigh on February 9. The left stump and right extremity showed no subsequent signs of necrosis and sufficient collateral channels were assumed to have been established. To relieve pain from the "phantom left limb," lumbar block and division of sciatic trunks were performed on June 16. Subsequently the patient showed a steady decline with continuous loss of blood from the gastrointestinal tract via rectum.

The thorax was opened within two hours after death (August 28, 1942) and approximately 1 quart of pantopaque-latex injected by means of a Janet-Frank's bladder syringe connected to a cannula in the descending thoracic aorta. The pigmented injection medium filled all the arteries to the gastrointestinal tract and some of the medium was observed to enter the lumen of the proximal part of the jejunum. The right posterior tibial artery was exposed and found to contain pigmented injection medium, verifying the completeness of the injection. The liver, stomach, small (except duodenum and upper part of jejunum) and large intestine were removed. Roentgenograms of the entire specimen were taken and the specimen fixed in acetic acid embalming solution (pH 2.6) by immersion and "punch-embalming" for later dissection.

At the time of death the vessels involved in supplying the right extremity and the cause of loss of blood from the gastrointestinal tract (via rectum) were not ascertained. It was tentatively assumed that collateral circulation through dilated hemorrhoidal vessels might play a part, if the right iliac vessels were occluded. Roentgenograms showed, however, that the proximal part of the jejunum (Fig. 4—at point of clamp), the aneurysm of both the aorta and right iliac artery and all the pelvic branches of the latter, as well as arteries of the right extremity were filled with the contrast medium. The left common iliac artery was completely occluded, but the left hypogastric artery and its branches were patent (Fig. 5). No dilatation of the hemorrhoidal vessels could be observed.

Subsequent dissection demonstrated that the ligatures had cut through the aortic walls and were embedded in an aneurysm, which developed after ligation, proximal to the origin of the inferior mesenteric artery. This second aneurysm had extended over the point of ligation and produced a new channel through which blood could flow distally. A perforation into the jejunum, near the duodenojejunal junction, was found which formed a direct communication from the aneurysm, above the inferior mesenteric, into the gastrointestinal tract.

As indicated in these figures and verified by dissection, the vessels to the right limb had patent lumina, as shown by their containing red latex, whereas lumbar and sacral arteries of the left side formed collateral channels to the left hypogastric artery, the branches of which were slightly enlarged but normal in their distribution. Even the smaller arteries, such as the lateral sacral, were filled with the latex mixture and their course and anastomosis could be dissected with ease.

Although in the present emergency there may be a scarcity of latex, biological supply houses or other depots may have sufficient stores to warrant the use of this injection medium for studies as describd.

SUMMARY

Ethyliodophenylundecylate (pantopaque) emulsified with pigmented liquid latex is an ideal injection medium for studies of the vascular system where the course of main or collateral vessels has been occluded by disease or surgical intervention. Roentgenograms of the vessels can be obtained and their course ascertained by dissection.

I am greatly indebted to Dr. J. J. Morton and Dr. W. J. M. Scott of the Department of Surgery and Drs. S. L. Warren and W. H. Strain of the Department of Radiology for making the material available and for their cooperation in this study.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

DOUGLAS, B. H., and BIRKELO, C. C.: Screening for tuberculosis in civilian population by fluorography 390

BAILEY, W.: Technic for chest x-ray examinations of large groups. I. The use of standard size films 390

BAILEY, W.: Technic for chest x-ray examinations of large groups. II. The use of miniature films 390

KERR, W. J.: Faulty movements of the diaphragm as a cause of non-obstructive emphysema and angina pectoris 391

ALLISON, S. T.: The vanishing lung 391

KARAN, A. A., and SINGER, E.: Transitory pulmonary infiltrations mistaken for tuberculosis 391

REEVES, R. J., SMITH, D. T., and BAKER, R. D.: Tuberculous pneumonia of lower lobe of right lung 392

PERRONE, J. A., and LEVINSON, J. P.: Primary carcinoma of the lung 392

OCHSNER, A., and DEBAKEY, M.: Carcinoma of the lung 392

SCOTT, W. G., and LIONBERGER, J. R., JR.: Studies of pulmonary vessels by means of body-section radiography 394

STANFORD, W. R., and NALLE, B. C., JR.: Cystic disease of the lungs 394

WINN, W. A., and JOHNSON, G. H.: Primary coccidioidomycosis 394

ATTWOOD, C. J., and SARGENT, W. H.: Cystic fibrosis of the pancreas with observations on roentgen appearance of associated pulmonary lesions 395

SWINEFORD, O., JR., and HARKRADER, C. J., JR.: Intrathoracic lipoma 395

KORNBLUM, D.: Attempt at roentgenographic visualization of thoracic duct and cisterna chyli 396

WHITCOMB, B. B., and SCOVILLE, W. B.: Postoperative chylothorax 396

Abdomen

BLACKFORD, S. D., BIRD, R. M., JR., and CASSCELLS, S. W.: Non-operative results in ninety patients with abnormal cholecystograms 396

HOFFMAN, H. S.: Benign hepatoma 396

BOWERS, R. F., LORD, J. W., JR., and McSWAIN, B.: Cystadenoma of pancreas 397

RABINOVITCH, J., and PINES, B.: Cysts of the pancreas 397

FAUST, D. B., and BRANDSTADT, W. G.: Case of pancreatic lithiasis 398

PUGH, D. G.: Roentgenologic aspect of pseudomyxoma peritonaei 398

SIMEONE, F. A.: Perinephric abscess 398

STEINBERG, C. L.: Value of splenectomy in Felty's syndrome 399

GIBB, W. T., JR.: Theory concerning manner in which the stomach empties itself 399

BISGARD, J. D., MATSON, G. M., and HIRSCHMANN, J.: Adynamic ileus and thermal influences on gastric and intestinal motor activity 399

DUDLEY, G. S., MISCALL, L., and MORSE, S. F.: Benign tumors of the stomach 400

POPPEL, M. H., and STARR, S.: Roentgen manifestations of acute infectious mononucleosis in the abdomen 401

SMEDAL, M. I.: Pyloric ulcers 401

POPPEL, M. H., and BERCOW, C.: Perforation of peptic ulcer 401

STEIGMANN, F.: Treatment of large gastric ulcers 401

FALK, V. S.: Familial polyposis of the colon 402

HENDERSON, S. G., and BRIANT, W. W., JR.: Colon in the healthy newborn infant 402

BOUSLOG, J. S. Normal stomach and small intestines in the infant 403

DEAMER, W. C., and CAPP, C. S.: Clinical aspects of gastro-intestinal disease in childhood 403

SPIESMAN, M. G., and RUBENSTEIN, H. I.: Hodgkin's lymphogranuloma (rectal stricture) 403

MENNE, F. R., MASON, D. G., and JOHNSTON, R.: Lymphosarcoma of intestine 404

MILLER, E. R., and HERRMANN, W. W.: Argentaffin tumors of small bowel 404

Skeletal System

SUSSMAN, M. L., and COPLEMAN, B.: Roentgenographic appearance of bones in Cushing's syndrome 404

CONNOR, P. J., and MAIER, F. J.: Value of roentgen rays in diagnosis of endocrine diseases 405

BARDEN, R. P., *et al.*: Ewing's endothelial myeloma with extensive skeletal involvement 405

LEVITT, A., and LEVY, D. S.: Multiple myeloma 406

MENVILLE, L. J., WILLIAMSON, L., and MATTINGLY, D.: Renal rickets 406

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

Douglas, Bruce H., and Birkelo, Carl C. Screening for tuberculosis in a civilian population by fluorography. *Ann. Int. Med.*, Nov., 1941, *15*, 853–857.

A rather common procedure for survey of pulmonary tuberculosis includes tuberculin skin testing to identify those who at some time may have been infected with the tubercle bacillus; thereafter, roentgenographically examining the chests of all positive skin reactors.

The authors have inventoried other possibilities which might provide for more direct information and money savings. They have considered the full-size standard film but have concluded it to be too expensive; they have considered sensitized paper—less costly but still too expensive; they object to fluoroscopy because of its not providing a permanent record and because of Fellows' statistics which have indicated approximately a 13 per cent error for it versus the standard film; they believe that the 35 millimeter film sacrifices too much accuracy in favor of economy. They have concluded that a 4×5 inch fluorograph is reasonably accurate, the single image study incurring no more than 2.6 per cent error as compared with the standard 14×17 inch film studies. They recommend this procedure as practical for group surveys and substantiate their contentions on the basis of 30,000 examinations. Some of these have been studied by skin testing also. Of 47.6 per cent who reacted positively, there were 3 active cases; whereas, among 671 who reacted negatively, there were 2 active cases. A number of those who were inoculated with tuberculin failed to return for re-examination.—*A. A. de Lorimier.*

Bailey, Wilbur. Technic for chest x-ray examinations of large groups. I. The use of standard size films. *Radiology*, Sept., 1942, *39*, 306–309.

Roentgen examination of large groups of people for tuberculosis is becoming increasingly popular and of course is used for the examination of Army recruits. Films of substandard size and film substitutes have been used in an attempt to reduce the cost of such examinations and the impression has been given in some quarters that satisfactory results and sufficient speed could not be attained with standard 14×17 inch films. The author maintains that this is not true and describes the technique of examination used at the Los Angeles Army Induction Station. The greater part of the time required for any mass survey is consumed in measuring and placing the patients and therefore this method can be made as rapid as any of those that use substandard films, paper rolls, etc., while the films are of much better quality.

Reports in the German literature say that 300 men can be examined per hour but the author has found that for good work not more than 100 can be examined as a matter of routine. More than 125 per hour were examined when the subjects were medical students, as they gave more intelligent cooperation.—*Audrey G. Morgan.*

Bailey, Wilbur. Technic for chest x-ray examinations of large groups. II. The use of miniature films. *Radiology*, Sept., 1942, *39*, 310–313.

The technique used for mass examinations with 4×5 and 4×10 inch films does not differ greatly from that with standard films. The target-film distance is decreased, however, and the kilovoltage increased, while the milliampere-second output must rise to 40 to 60 ma-sec., or even more. These changes tend to produce poorer detail and contrast in the image. But though the detail is less than on standard films a comparison of a large number of cases examined with standard films and an equally large number with 4×10 inch films showed that a somewhat larger number of cases of tuberculosis was revealed by the 4×10 inch films than by the standard films.

Another disadvantage of the small films lies in the fact that the long exposure time required is apt to produce a simulated enlargement of the heart and great vessels and it is hard to tell whether there is an actual enlargement. But as

a whole the results are better than might be expected for mass examinations for tuberculosis. —*Audrey G. Morgan.*

Kerr, Wm. J. Faulty movements of the diaphragm as a cause of non-obstructive emphysema and angina pectoris. *Radiology*, August, 1942, *39*, 153–156.

The author maintains that non-obstructive emphysema and apparent angina pectoris are often brought on by faulty movements of the diaphragm due to obesity. He has very successfully treated such cases of chronic bronchitis with emphysema and relieved the orthostatic dyspnea and cough by the use of an abdominal belt which is illustrated. This supporting belt acts as a means of artificial respiration and helps to restore the function of the diaphragm. Kountz and Alexander recommended the use of a firm supporting belt to hold up the pendulous abdomen and aid in the movements of the diaphragm. The author modified this belt by adding elastic segments at the sides to insure freer movement of the diaphragm.—*Audrey G. Morgan.*

Allison, Stanton T. The vanishing lung; report of a case of advanced bullous emphysema. *Ann. Int. Med.*, July, 1942, *17*, 139–148.

Pulmonary emphysema is a condition of the lungs brought about by overdistention of the walls of the alveoli resulting in loss of elasticity and finally rupture. This may produce such pressure on the lung tissue that it is almost entirely destroyed.

A case is described in a man of forty-one who complained of a severe chest cold with pain and dyspnea. He had had epilepsy since childhood with infrequent attacks of petit mal. He had had pneumonia twice before he was ten years of age. While in college in 1917 his chest expansion had been 4 inches; in 1940 on taking an examination for conditioning he was found to have no chest expansion at all but in spite of that was allowed to take the strenuous conditioning exercises, after which he suffered from severe and long-continued dyspnea. For some months he had been unable to sleep on his left side without cough and dyspnea.

Stereoscopic roentgenograms of the chest showed no lung markings in the right chest except a few cobweb-like strands at the base. The upper half of the left lung showed the brilliance characteristic of absence of lung tissue but the markings of the lower half of the left field were increased. When he slept on his left side he splinted the only part of the lung that was functioning and so of course became dyspneic.

This patient had had frequent respiratory infections during childhood and had had what he called a cigarette cough for years. Emphysema is caused by strain on the walls of the alveoli due to coughing in patients with asthma, chronic bronchitis and other chronic pulmonary diseases. The popular theory that it is caused by glass blowing or the blowing of wind instruments is false.

The patient was advised to go to Tucson, Arizona, where the clear, dry air will lessen the danger of respiratory infections, to avoid strenuous exercise and heavy lifting and be at least very moderate in the use of tobacco and alcohol, as the former would further irritate the bronchi and the latter would increase the pulse rate and lower his resistance. A diet low in fats and carbohydrates but high in proteins, vegetables, fruits and vitamins was recommended with the use of an abdominal belt to increase intra-abdominal pressure, elevate the diaphragm and increase vital capacity. If these directions are followed it is believed he may live for years even with his limited lung capacity.—*Audrey G. Morgan.*

Karan, A. A., and Singer, Emanuel. Transitory pulmonary infiltrations mistaken for tuberculosis, with a report of five cases. *Ann. Int. Med.*, July, 1942, *17*, 106–124.

Recently increasing dependence has been placed on the diagnosis of pulmonary tuberculosis by roentgen examination. Five cases are described which show that roentgenograms of themselves are not entirely reliable, particularly a single examination. A series of examinations should always be made. If tubercle bacilli cannot be found in the sputum or stomach contents by microscopic examination, cultures or guinea pig inoculation, the case is probably not one of tuberculosis. This is important as artificial pneumothorax, which is useful in the treatment of tuberculosis, may be useless or even harmful in other conditions.

The roentgenograms in the 5 cases described which were accepted as typical of tuberculosis by competent roentgenologists and phthisiologists, are reproduced. But serial examinations showed the incorrectness of the diagnosis as the lung infiltrations cleared up.

Two of the cases were bronchopneumonia probably caused by a filtrable virus. In 1 case the infiltration and rarefaction seen on the first roentgenogram were thought to be due to a lobular atelectasis with beginning necrosis of the lung resulting from bronchial obstruction. The other 2 cases showed eosinophilia and were probably allergic in character. The agent that caused the allergic reaction was not determined. In 1 of the cases the pulmonary exudate had persisted long enough to cause increased resistance in the pulmonary circulation, resulting in enlargement of the right ventricle which returned to normal size when the exudate was absorbed.—*Audrey G. Morgan.*

Reeves, Robert J., Smith, David T., and Baker, Roger D. [Tuberculous pneumonia of lower lobe of right lung (primary focus).] *Radiology*, Oct., 1942, *39*, 467–473.

The case considered at this clinico-pathological conference was that of a white grocery salesman admitted to the hospital because of fever of six weeks' duration. Unusual features of the case were that he had a fever four months before admission that was mistaken for malaria. Six weeks before admission he had an acute respiratory infection with yellow sputum that was reported as foul. Four days before admission he had red swollen ankles with erythema. There was a persistent neutropenia with nonsegmented polymorphonuclear cells, suggesting leukemia, nodes in the right hilar region, a spreading pulmonary lesion, an enlarged spleen, a continuous high fever (39° to 40° C.) with bradycardia followed by tachycardia and a terminal gangrene of the cheek. The patient died sixty-nine days after admission to hospital.

The possible diagnoses to be considered were tuberculosis, metastatic carcinoma from some unknown origin, primary bronchogenic carcinoma, Hodgkin's disease, aleukemic leukemia, myelogenous leukemia. Autopsy showed tuberculosis, but not the usual type of adult tuberculosis with predominant involvement of the apices with nodules or cavities. It rather resembled the primary tuberculosis of childhood. Apparently the patient became infected with tuberculosis only a few months before death. The caseous pneumonia of the right lower lobe represented the primary focus, this spread to the hilar nodes causing the mass. Hematogenous spread occurred to an extent that justified the term miliary tuberculosis. The fusospirochetal gangrene of the right cheek was a terminal incident not connected with the primary disease.—*Audrey G. Morgan.*

Perrone, J. A., and Levinson, J. P. Primary carcinoma of the lung (report of 115 cases, 38 autopsies and 77 bronchoscopic biopsies). *Ann. Int. Med.*, July, 1942, *17*, 12–25.

The authors present a study of 38 cases of primary carcinoma of the lung found on autopsy and 77 cases diagnosed by bronchoscopic examination at Mercy Hospital, Pittsburgh, from 1911 to 1939.

Many forms of chronic irritation of the lung seem to cause cancer. There are about 3 cases in males to 1 in females and the proportion of women has not increased in recent years in spite of the fact that women smoke a great deal more. The total incidence of carcinoma of the lung has increased quite rapidly since the beginning of the century. The age of the patients in this series was from twenty-three to seventy-six. These tumors seem to be relatively rarer in the Negro than in the white race.

About 70 per cent of the cases originate in the bronchi, and bronchoscopy is the one certain method of diagnosis. The physical findings may simulate those of any kind of lung disease. The chief roentgen finding is atelectasis of the lung. There was superimposed inflammation in about 27 per cent of these cases. Diagnosis cannot be made by roentgen examination alone.

The four cardinal symptoms are cough, hemoptysis, pain and dyspnea. Every family physician should know that in any case of indefinite disease of the lung a most thorough examination should be made for carcinoma. If bronchoscopic and bioscopic examinations were made in all such cases these tumors would be detected much earlier when the prospects for successful treatment are better.

Only 30 of the 77 cases examined in this series were operable and only 1 of them is alive three years after pneumonectomy. Surgery, however, is the treatment of choice as neither roentgen irradiation nor implantation of radium is very effective.—*Audrey G. Morgan.*

Ochsner, Alton, and DeBakey, Michael. Carcinoma of the lung. *Arch. Surg.*, Feb., 1941, *42*, 209–258.

Recently early diagnosis and improved surgical management have rendered the prognosis in carcinoma of the lung relatively favorable as

compared with earlier cases, diagnosed late and treated with inadequately developed preoperative, anesthetic and operative techniques. This disease has become a significant problem in cancer therapy; its incidence is increasing, absolutely, to be second only to cancer of the stomach (autopsy series).

Among the various suggested etiologic agents, insufficient evidence exists to incriminate influenza, tuberculosis, syphilis and inhalation of tar and benzene products.

The importance of nonspecific pulmonary infections, bronchiectasis and chronic bronchitis, pneumoconiosis and trauma is doubtful. Smoking, especially cigarette smoking associated with inhaling, is largely accountable for the increased incidence of pulmonary carcinoma in the authors' opinion.

Three-fourths of the cases are in males; four-fifths are between the ages of forty and seventy, but cases occur as early as the first decade.

Carcinoma of the lung is bronchogenic in origin, arising centrally in most instances. A logical classification of these neoplasms is Halpert's based on the development of the lining cells of the bronchus. According to this explanation, carcinomas arise by atypical proliferation from "reserve cells" (normally found beneath and developing into the ciliated cylindrical and goblet cells) to result in (1) "reserve cell," (2) cylindrical cell, or (3) squamous cell carcinoma. Metastasis occurs by direct extension, through lymphatics, through blood stream and by "bronchial embolism." Metastatic sites, in order of frequency are: regional lymph nodes (75.9 per cent), liver (33.4 per cent), bone (20.4 per cent), adrenals, kidney, brain, heart and pericardium, and pancreas. The need for removal of regional nodes at the time of operation is evident.

Bronchial carcinoma presents no characteristic symptomatology; the onset is usually insidious; the most constant symptom is cough, non-productive at first, later becoming productive of mucoid, mucopurulent, blood tinged (hemoptysis is infrequent, however) or even foul sputum. Symptoms of an acute respiratory infection or indefinite thoracic pain are fairly frequent first symptoms; dyspnea is a late complaint, as are weight loss, weakness, cyanosis and pulmonary osteoarthropathy. Peripherally located tumors may produce evidences of pleurisy with effusion. Carcinoma of the lung must be seriously considered in any patient past the age of forty who exhibits respiratory symptoms; lung abscess without apparent cause should be counted of malignant origin until proved otherwise. The interval between onset of symptoms and death is usually cited in terms of months, but such an apparently rapid course is not necessarily an indication of the true duration of the symptoms. Physical findings are also varied; obvious physical signs usually signify inoperability.

A high index of suspicion is necessary for the early diagnosis of bronchial carcinoma. "Whereas roentgenographic examination without the use of contrast mediums is usually of little or no value in the *early* diagnosis of non-obstructive bronchial neoplasms; careful stereo-roentgenographic studies are necessary for all such lesions. The roentgen interpretation of centrally located lesions is generally more difficult because of the confusion with hilar shadows produced by other lesions and by normal structures. This is particularly significant because most pulmonary neoplasms occur in the hilar region." Later, atelectasis develops due to bronchial obstruction by the carcinoma. The high incidence of correct diagnosis by roentgen examination indicates the value of this procedure; tomographic studies are reported of value. Bronchoscopy and biopsy yield a positive diagnosis in over 70 per cent of the cases. Bronchography is an additional, important means of diagnosis. Malignant cells can be recognized in sputum or pleural fluid by a pathologist trained in such methods. Aspiration biopsy carries with it the probability of spreading metastases to the pleura.

The only curative treatment of pulmonary carcinoma is total surgical extirpation of the involved lung; excision of regional nodes is necessary. Irradiation "is of value in hopeless cases in alleviating the manifestations." Ten days to two weeks preliminary to pneumonectomy artificial pneumothorax is instituted to compress the pulmonary capillary bed gradually and allow complete compensation of the cardiovascular system before operation; this procedure also permits the determination of the presence and extent of adhesions.

The authors state their preference for cyclopropane inhalation anesthesia under positive pressure, an anterior approach and individual isolation of hilar structures. In 94 collected cases 38 patients recovered and 56 (59.5 per cent) died; of 24 patients in whom massive

ligation of hilar structures was done, 5 patients recovered from the operation and 19 (79.1 per cent) died; of 54 patients in whom individual ligation of hilar structures was done, 25 recovered and 29 (53.7 per cent) died.—*Henry G. Moehring.*

Scott, Wendell G., and Lionberger, John R., Jr. Studies of the pulmonary vessels by means of body-section radiography. *Radiology*, August, 1942, *39*, 157–165.

The pulmonary vessels can be visualized better by means of body section roentgenography than by conventional roentgenography because the former method blurs out the unwanted shadows and leaves only the structures that are of interest in clear relief.

Kieffer and Moore's laminagraph was used in making a series of body section roentgenograms which are reproduced. First a series of conventional films was made in the postero-anterior, right and left anterior oblique and left lateral positions. By analyzing the location of the pulmonary vessels on these films it was possible to determine the approximate levels in the various positions in which the sectional films were to be made. This provides a set of conventional films and one of sectional films of the pulmonary vessels for comparison. The spiral method was used to get maximum blurring of unwanted shadows.

The size and degree of dilatation of the pulmonary vessels, particularly the arteries, are best shown in lateral sectional films. Dilatation is the only reliable objective sign of disease of the pulmonary arteries. It is primarily the pulmonary veins that are dilated, the arteries only slightly so, in patients with mitral stenosis and insufficiency from rheumatic heart disease.

There is a great deal of variation in the normal size, shape, position and course of the pulmonary vessels. The pulmonary veins are harder to visualize than the arteries because they are smaller, have shorter main trunks and are therefore in closer contact with the heart.

It is hoped that this method of body section roentgenography will stimulate closer study and observation of the pulmonary circulation, resulting in a deeper knowledge of its diseases. —*Audrey G. Morgan.*

Stanford, W. R., and Nalle, Brodie C., Jr. Some notes on cystic disease of the lungs, with a report of one case. *Ann. Int. Med.*, July, 1942, *17*, 65–77.

A case of cystic disease of the lungs seen in Duke Hospital is described and illustrated with photographs of the autopsy specimens and roentgenograms. The chief emphasis is laid on the difficulty of differential diagnosis between congenital cysts, acquired cysts and extensive emphysema with formation of bullae. The differentiation is important as some forms of cyst of the lung can be treated surgically.

The patient was a Negro of thirty-four who complained of shortness of breath and indigestion which had begun about four years before. He had slight wheezing at times and one physician had diagnosed the condition as asthma. These cases may present a marked resemblance to asthma.

Roentgen examination showed cysts in the left mid lung and throughout the right lung. The picture resembled that of congenital cystic disease of the lungs. An attempt was made to do a diagnostic pneumothorax on the right chest but unfortunately a spontaneous pneumothorax developed, the patient became much more dyspneic and died five days later.

The pathologist reported that this resembled a case of acquired pulmonary emphysema. There is nothing in the history to indicate that the patient had any pulmonary malformation before the age of thirty. The most likely explanation seems to be that the elastic tissue of the lung was poor in quality and that at the age of thirty it had deteriorated so much that this extensive emphysema developed.

Lack of pigment in the wall of a cyst is the only thing to show that it is congenital. But in this case there was no fluid in the cysts; they all contained air and therefore naturally pigment. An absolute diagnosis of congenital cyst cannot be made without roentgen evidence of such a lesion at birth.

The mortality in these cysts is high. Infection is a serious complication. Of course if too much lung tissue is destroyed no medical or surgical treatment will do any good.—*Audrey G. Morgan.*

Winn, William A., and Johnson Gilbert H. Primary coccidioidomycosis; a roentgenographic study of 40 cases. *Ann. Int. Med.*, Sept., 1942, *17*, 407–422.

Human infection with *Coccidioides immitis* was first recognized fifty years ago but up until five years ago only the chronic disseminating form—coccidioidal granuloma—which has a

mortality of 50 to 60 per cent, was recognized.

In 1937 Dickson identified the benign primary form of the infection known as valley fever, which is endemic in the San Joaquin Valley of California, in Arizona and probably in other dry and dusty areas. The incidence of the disease will increase as more soldiers are sent to these regions. Transmission is by inhalation of the vegetative stage of the fungus with dust. It is not, so far as is known, transmitted from person to person or from animal to animal.

There are no pathognomonic symptoms of the beginning of the infection. The symptoms resemble those of influenza or pneumonia or a severe cold. The characteristic erythema nodosum occurs in only about 2 to 5 per cent of the cases. The roentgen and anatomic changes resemble those of tuberculosis, and in cases of suspected tuberculosis in which tubercle bacilli cannot be found in the sputum the possibility of coccidioidal infection should be considered. In most of the cases presented in this article *Coccidioides immitis* could be isolated from the sputum and there were positive skin reactions to coccidioidin. Roentgenograms of the authors' 40 cases are given.

The mortality of primary coccidioidomycosis is low as it does not generally become progressive. When it does assume the acute disseminating form it is probably always fatal and may run its course in from five weeks to seven months. A photograph is given of the most virulent case they have seen, in a Filipino, thirty-six years of age. There were multiple miliary verrucous skin lesions over the face, upper trunk and limbs.—*Audrey G. Morgan.*

Attwood, C. J., and Sargent, W. H. Cystic fibrosis of the pancreas with observations on the roentgen appearance of the associated pulmonary lesions. *Radiology*, Oct., 1942, *39*, 417–425.

Cystic fibrosis of the pancreas in infants and young children is not extremely unusual though its diagnosis is. The authors report 4 cases discovered in 125 consecutive autopsies. In only 1 of these cases was the correct diagnosis suspected from the clinical or roentgen findings.

The etiology of the pancreatic lesions is not definitely known but Andersen believes they are due to obstruction of small or large pancreatic ducts. Though no etiological relationship has been proved between the pancreatic and lung changes it is believed that if the association of this pancreatic disease with definite changes in the lungs were more widely known it would be possible to make the diagnosis more frequently from roentgen examination of the lungs. The best clinical method for the confirmation of the diagnosis is the demonstration of the absence of pancreatic trypsin and lipase in the duodenal juice. The lung changes, as described and illustrated in these cases, consist essentially of purulent bronchitis with bronchiectasis and bronchiectatic abscess formation and surrounding pneumonitis.The changes are most marked around the hilum, decreasing in intensity toward the periphery.

The authors' patients ranged in age from three months to two years which is about the usual age for this disease. Therefore it is in this age group that the pulmonary changes described are most apt to be associated with cystic fibrosis of the pancreas.—*Audrey G. Morgan.*

Swineford, Oscar, Jr., and Harkrader, Charles J., Jr. Intrathoracic lipoma. *Ann. Int. Med.*, July, 1942, *17*, 125–129.

Only 25 cases of wholly intrathoracic lipoma have been reported. The authors report a case in a man of sixty-two admitted to the Hospital of the University of Virginia in severe status asthmaticus with congestive heart failure which had lasted for ten days. For twenty-five years he had had asthma whenever he contracted an acute respiratory infection. Attacks had been relieved in 1937 and 1939 by bronchoscopy. On this admission, bronchoscopy was followed by a severe attack of asthma with shock, and the patient remained semi-comatose with frequent periods of Cheyne-Stokes respiration, cyanosis and pulmonary edema for six days and then died.

Autopsy showed a large lipoma filling the base of the right thorax. The lipoma was not necessarily the primary cause of the asthma. Bronchial stenosis is known to be a cause of asthma and in this case there was stenosis of the middle lobe bronchus, apparently caused by inflammation and not by pressure from the tumor. The middle lobe had apparently not functioned for a long time as shown by the absence of pigment, and this suggests further doubt as to whether the asthma was caused by the lipoma. In a collection of 19 cases reviewed from the literature 5 showed some symptoms of asthma.

Roentgenograms taken during the final illness showed a mass above the diaphragm but they did not show the decreasing density of the shadow from the center toward the periphery which is characteristic of intrathoracic lipoma. This finding was seen to a certain degree in roentgenograms taken in 1937.—*Audrey G. Morgan.*

Kornblum, Daniel. Attempt at roentgenographic visualization of the thoracic duct and cisterna chyli; theoretical considerations and preliminary observations. *Radiology*, Oct., 1942, *39*, 395–399.

A large part of the fats absorbed from the intestine passes through the lacteals and thoracic duct. It seemed to the author, therefore, that it might be possible to get a sufficient concentration of iodine in the thoracic duct and cisterna chyli following the ingestion of iodized oil so that they could be demonstrated roentgenographically. He reviews the anatomy of the duct and cistern and describes studies made with iodipin and lipiodol in an attempt to visualize them. But a shadow conforming to the anatomic position and size of the duct was seen in a roentgenogram of the chest in only 1 out of 12 subjects after the administration of iodized oil. Further observations with lipiodol, however, failed to confirm this structure as a part of the thoracic duct. Further tests of the method are in order.—*Audrey G. Morgan.*

Whitcomb, Benjamin B., and Scoville, William B. Postoperative chylothorax. *Arch. Surg.*, Nov., 1942, *45*, 747–753.

A case is described in a woman of thirty-nine in which sympathectomy was performed for hypertension. She was extremely emaciated and in the course of the operation the thoracic duct was torn. No attempt was made to suture it but silver clips were placed on both the proximal and distal ends. The proximal end reopened after seven to ten days and repeated thoracentesis was necessary in order to remove the chyle. On the seventeenth day after operation it was decided to reinject the citrated chyle. The patient died within a few minutes of the beginning of the infusion. She presented asthma, dyspnea, cyanosis, chills and shock. Autopsy was not permitted so it was impossible to say definitely whether death was caused by anaphylaxis, fat embolism, or a foreign protein reaction but the clinical picture indicated anaphylaxis as the cause of death.

This method of treatment has been used in 6 cases of postoperative chylothorax and 3 of the patients have died. They generally die of inanition rather than respiratory embarrassment.

Intravenous injections of fat and protein should be given early in chylothorax to prevent rapid emaciation. If intravenous administration of chyle is used in the future the patient's sensitivity should be carefully tested with an injection of 5 to 10 cc. and the infusion proper delayed for half an hour. The fat globules should be measured microscopically and specimens containing globules over 3 microns in diameter should be rejected; twenty-four hour cultures of the chyle should be made.—*Audrey G. Morgan.*

ABDOMEN

Blackford, Staige D., Bird, Robert M., Jr., and Casscells, S. Ward. Non-operative results in ninety patients with abnormal cholecystograms. *Ann. Int. Med.*, June, 1942, *16*, 1118–1122.

Records of 500 abnormal cholecystograms were found in the files of the Department of Roentgenology of the University of Virginia. Among the patients represented by these, 252 were operated on. Ninety patients not operated on were followed up for an average time of six and a half years. The average age of the patients was 50.3 years. In 25 of the cases the symptoms were mild, in 26 moderate and in 37 severe. In 2 cases the records were not sufficient to grade the severity of the symptoms.

After an average period of six and a half years medical, or rather non-surgical treatment, the results were satisfactory in 47.7 per cent of the entire 90 cases, in 52.5 per cent of those with poor function and 44.9 per cent of those with no function and in 42.8 per cent of those with cholelithiasis.

Conceding the disadvantages of questionnaire follow-up of patients and the small number of the cases, the authors still believe that these results indicate that the patient with uncomplicated cholecystitis should be given a trial on medical treatment and if not promptly relieved he should be operated on.—*Audrey G. Morgan.*

Hoffman, H. S. Benign hepatoma. *Ann. Int. Med.*, July, 1942, *17*, 130–139.

Benign tumors of the liver are very rare and apparently only 58 cases have been described in

the medical literature of the world. They rarely cause symptoms unless they become large enough to cause signs of pressure on the liver or neighboring organs.

The author describes a case in a woman of thirty-eight and reviews 3 cases from the literature. His own patient came for treatment of a mild respiratory infection but said that recently she had been conscious of a sensation in her right upper abdomen, though there was no pain and she had no other symptoms referable to it. She thought she felt a mass in the right upper quadrant. Roentgenograms showed such a mass with a rounded lower pole. They did not show whether it was a prolongation of the liver or a separate mass.

Operation showed a firm nodular tumor projecting from the lower surface of an apparently normal liver. The tumor was shelled out with only moderate loss of blood. Microscopic examination showed liver tissue presenting portal cirrhosis with active hepatitis and hyperplasia of bile ducts.

It is impossible to say whether this tumor developed from a congenital cell rest which later became inflamed or whether an area of focal necrosis became localized as an extrahepatic tumor. None of the cases heretofore described has shown this association of apparently normal liver tissue with an active pathological process in a histoid tumor.—*Audrey G. Morgan.*

Bowers, Ralph F., Lord, Jere W., Jr., and McSwain, Barton. Cystadenoma of the pancreas. *Arch. Surg.*, 1942, *45*, 111–122.

Descriptions are given of 5 cases of cystadenoma of the pancreas treated at the New York Hospital in the past nine years. The patients were all women, ranging in age from thirty-seven to sixty-six years. Four of them had a history of disease of the bile tract and in 4 of them there was a visible, palpable mass in the left upper quadrant of the abdomen. Roentgen examination showed this mass and a gastrointestinal series showed displacement of the stomach and transverse colon. An intravenous pyelogram in 1 case showed poor function of the left kidney, probably due to pressure of the cyst on the renal artery or vein, as it disappeared after operation. Three of the patients had diabetes which improved after operation in 1 case and was readily controlled by insulin in all.

The splenic vein is dilated and intimately related to the wall of the cyst in these cases. In 1 case injury to this vein during the operation caused the death of the patient. The other patients are all living and well up to as much as two and a half years after the operation.

Photomicrographs show the typical picture of cystadenoma of the pancreas.—*Audrey G. Morgan.*

Rabinovitch, J., and Pines, B. Cysts of the pancreas. *Arch. Surg.*, 1942, *45*, 727–746.

Seventeen cases of cysts of the pancreas seen at the Jewish Hospital in Brooklyn are described and illustrated with photomicrographs.

Eleven of the cases were pseudocyst, 2 cystadenoma, 2 retention cyst, 1 inclusion cyst and 1 pseudocyst with malignant degeneration, which is rare. Inclusion cyst is a form not heretofore described in the literature. It originates from Brunner's glands included in the pancreas as a result of some defect in embryonic development.

These cysts are usually seen in middle life. The ages of these patients varied from twenty-one to seventy-six years, the average being 45.4 years. Fourteen were females and 3 males. There is some evidence to show that trauma is a factor in the causation of these cysts. Cholecystitis and pancreatitis are also etiological factors.

Diagnosis is rather difficult as the symptoms resemble those of other intra-abdominal tumors. The presence or absence of pancreatic enzymes in the cyst fluid is not conclusive. The patients generally have a history of transient attacks of pain and some of them show loss of weight, constipation or diarrhea, nausea and vomiting and jaundice. The cysts, as a rule, are relatively immobile, though when they are in the tail of the pancreas they may be freely movable. Roentgen examination is of great value. If the tumor is in the head of the pancreas the duodenal curve is enlarged and there are definite changes in the angle of the duodenum. Displacement of the duodenum and small intestine indicates cyst of the pancreas. In 6 of the patients in this series roentgen examination showed a mass in the region of the pancreas.

The correct diagnosis was made in 4 cases before operation; mistaken diagnoses included carcinoma of the pancreas, retroperitoneal tumor, ovarian cyst or fibromyoma of the uterus, peptic ulcer, acute pancreatitis, acute cholecystitis, chronic appendicitis and retroperitoneal sarcoma or cyst of the pancreas.

The ideal treatment is complete removal of the cyst if possible. If the cyst is large and adherent marsupialization is the treatment of choice. The prognosis is good in benign cysts but of course bad in the infrequent cases of malignant cyst.—*Audrey G. Morgan.*

Faust, D. B., and Brandstadt, W. G. A case of pancreatic lithiasis. *Ann. Int. Med.*, July, 1942, *17*, 148–152.

Though 113 or more cases of pancreatic lithiasis have been described only 4 have been diagnosed by roentgen examination before operation, and 30 during operation, as the symptoms are very indefinite.

A case is described in a Negro, aged forty-five, who had been hospitalized repeatedly for "stomach trouble" since 1918. He had severe epigastric pain which at first was not related to the taking of food but later was caused even by the sight or smell of food.

Films of the gastrointestinal series showed a solitary calcified nodule in the liver and fine and medium sized calcified areas in the region of the pancreas. Lateral and oblique views proved the calcifications were in the pancreas.

Surgery was advised but refused, but about eighteen months later the patient had an attack of such agonizing pain that he consented to operation. One small white calculus was removed from the pancreas, but others in the terminal ducts could not be removed. About ten weeks after operation there was a sudden return of pain, probably due to blocking of the pancreatic duct by another stone. Another operation has been advised, though it is doubted whether there is any hope for permanent cure with stones distributed as in this case. —*Audrey G. Morgan.*

Pugh, David G. A roentgenologic aspect of pseudomyxoma peritonaei. *Radiology*, Sept., 1942, *39*, 320–322.

Pseudomyxoma peritonaei is a condition in which masses of gelatinous or myxomatous material, usually originating from a pseudomucinous cystadenoma of the ovary or a mucocele of the appendix, are distributed over the surface of the peritoneum in the form of multiple cysts of various sizes. It has heretofore not been possible to diagnose this condition by roentgen examination but a case is described in a man of thirty-two in whom such a diagnosis was made at the Mayo Clinic. The roentgenograms showed many annular shadows of calcification throughout the abdomen, particularly in the pelvis. Also distributed throughout the abdomen but most marked in the upper part, were shadows of large masses of soft tissue.

Another case is described in a woman of fifty in which the roentgenogram was similar but in her case there was a questionable differential diagnosis from peritoneal paraffinoma. She had had several abdominal operations, and after the last one a bottle of some substance had been poured into the peritoneal cavity to prevent adhesions. It is questionable whether this was mineral oil which sometimes causes a chronic chemical peritonitis. At first the patient seemed to be benefited by roentgen treatment which would indicate pseudomyxoma rather than paraffinoma, but recently she has had no benefit from irradiation.

Roentgen examination is diagnostic in these cases only because of the multiplicity of the cysts and their wide distribution.—*Audrey G. Morgan.*

Simeone, F. A. Perinephric abscess. *Arch. Surg.*, Sept., 1942, *45*, 424–442.

The author divides cases of perinephric abscess into simple and complicated. In the former group the infection has reached the perinephrium from distant foci, but cases are also included in which it has reached it by extension from metastatic abscess or carbuncle of the kidney. Complicated abscesses are those that have reached the perinephrium by direct extension from diffuse pyelonephritis or pyonephrosis or by direct or lymphatic extension from adjacent or nearby foci.

Sixty-six cases seen at the Peter Bent Brigham Hospital in the past twenty-eight years are analyzed. If there is fever and pain in the flank perinephric abscess should be considered. Fever, leukocytosis, increased sedimentation rate of erythrocytes, and tenderness in the loin are almost always found. Roentgenograms and laboratory findings are only corroborative. Fixation of the kidney and diaphragm may be seen if the abscess is near the upper pole of the kidney but not necessarily if it is around the lower pole or anteriorly in the perinephrium. Anterior displacement of the kidney has also been reported but an abscess may be anterior and not cause this sign.

In roentgen examination great care must be exercised in exposing lateral films as a very

slight deviation from the true lateral may project the kidney shadow far from its true position and suggest displacement that does not exist.

These patients are generally in poor condition as the primary disease has existed for a long time. At the first operation as little as possible for adequate drainage of the abscess should be done. If drainage of the kidney or nephrectomy is necessary it should be done as a secondary operation.

Among the cases of simple perinephric abscess in this series there was no mortality resulting from the abscess. Two patients died from other causes. For the entire group the mortality was 15 per cent. The mortality in complicated perinephric abscess may be from 14 to 50 per cent. —*Audrey G. Morgan.*

Steinberg, Charles LeRoy. The value of splenectomy in Felty's syndrome. *Ann. Int. Med.*, July, 1942, *17*, 26–40.

In 1924 Felty described a disease characterized by polyarthritis of the atrophic variety, fever, secondary anemia, leukopenia, splenomegaly and tachycardia. The disease is a constitutional one with all the symptoms of chronic infection.

Three cases are described and roentgenograms of the joints and photomicrographs of the spleen and bone marrow given. The roentgenograms are very much like those of atrophic arthritis. The bone marrow may be either depressed or hyperplastic. If it is inactive of course splenectomy could be of no value but bone marrow stimulants should be used.

The bone marrow was hyperplastic in 2 of the cases here described. Though cells were produced in abundance by the bone marrow there was apparently some obstacle to their passing into the peripheral circulation. On the theory that this obstacle was the spleen splenectomy was performed in 1 of the cases. Operation was followed by improvement in the blood picture and general health. The arthritis was not affected. Two cases of operation for Felty's syndrome described in the literature were followed by death.—*Audrey G. Morgan.*

Gibb, William T., Jr. A theory concerning the manner in which the stomach empties itself. *Ann. Int. Med.*, Jan., 1942, *16*, 94–103.

The author reviews the various theories that have been advanced to explain the emptying of the stomach and discusses a theory of his own based on 750 stomach examinations made at St. Luke's Hospital and Knickerbocker Hospital, New York City, with the Wolf-Schindler flexible gastroscope between February, 1938, and September, 1940.

He does not believe that the peristaltic wave is powerful enough to eject the stomach contents. The pylorus is open practically all of the time and closes only for about a second after each emptying of the stomach. Apparently its only function is to prevent reflux from the duodenum.

Gastroscopic examination has shown a new structure in the stomach called the musculus sphincter antri, running at right angles to the long axis of the stomach just opposite the incisura angularis and extending about half way up the anterior and posterior walls. This musculus is not found postmortem and does not seem to be different histologically from the rest of the stomach wall. It seems to be a functional structure with some definite use in the function of emptying the stomach.

When the duodenum is in proper condition to receive the stomach contents or when the stomach contents are in proper condition to be passed on, this musculus sphincter antri contracts forcibly, dividing the stomach into two compartments. At this time what may be termed a systole of the antrum takes place and the liquid food is squirted into the duodenum under considerable pressure.

This theory cannot be proved with the apparatus now available. To prove that during the systole of the antrum hydraulic pressure is increased there as compared with that in the body of the stomach would require something much more sensitive than the double balloon apparatus.—*Audrey G. Morgan.*

Bisgard, J. Dewey, Matson, Guy M., and Hirschmann, Jerome. Adynamic ileus and thermal influences on gastric and intestinal motor activity. *J. Am. M. Ass.*, Feb. 7, 1942, *118*, 447–451.

The terms adynamic ileus and paralytic ileus are used to designate a condition characterized by distention and relative inactivity of the bowel. It was found that the Miller-Abbott tube traveled down the small bowel as readily and rapidly in the patient with so-called paralytic ileus as in the patient with normal intestinal function. For a logical explanation it

must be assumed that in a state of ileus the stretching of the bowel wall from distention is in large measure responsible for the lack of motor activity. Another incongruous situation is observed in the relief of ileus which may follow the paralysis induced by spinal anesthesia. By inducing paralysis, spinal anesthesia presumably releases the inhibiting action of the dorsolumbar sympathetic nervous system on the motor activity of the bowel and leaves the vagus unopposed. It is probable, therefore, that ileus results, at least in part, from an imbalance between the antagonistic actions of the dual innervation of the bowel. Complete paralysis of the bowel does occur in the presence of diffuse or generalized peritonitis.

The authors made continuous kymographic recordings of gastric and intestinal motor activity. These recordings registered the variations in pressure exerted on indwelling compressible rubber balloons by the peristaltic contractions of the viscera studied.

In previously reported studies it was shown that ether, nitrous oxide and barbiturates have an inhibiting action, while spinal anesthetics, cyclopropane and avertin with amylene hydrate have either a stimulating effect or no appreciable effect.

A detailed account of the influence of hot and cold applications on gastric and intestinal motor activity and on the secretion of hydrochloric acid was made in a previous communication. In the present study heat applied to the abdominal wall inhibited motor activity of the stomach, the small bowel and the colon, cold stimulated tonus and peristaltic activity. When heat or cold was applied directly to the wall of the stomach by having the patient drink hot or cold water the responses were reversed.

If it is beneficial, as is generally believed, to inhibit the motor activity of the gastrointestinal tract and thereby place it at rest as far as possible in the presence of inflammatory lesions, such as appendicitis and peritonitis, and of bleeding lesions, such as bleeding peptic ulcer, then hot applications and not ice bags are indicated. The increase in gastric acidity which follows chilling of the body surfaces may explain the recurrence of peptic ulcer in the fall and the spring, when there are rapid and radical changes in temperature.—*S. G. Henderson.*

DUDLEY, GUILFORD S., MISCALL, LAURENCE, and MORSE, STANLEY F. Benign tumors of the stomach. *Arch. Surg.*, Nov., 1942, *45*, 702–726.

There are various estimates as to the relative frequency of benign and malignant tumors of the stomach. Among 4,413 autopsies done at Bellevue Hospital in five years 22 per cent of all gastric tumors seen were benign. A comparison of the records of 76,077 adult medical and surgical patients admitted to the same hospital during three years and seven months showed that 456 had been operated on for tumors of the stomach and that only 6 of these, or 1.3 per cent, were benign. This difference between autopsy and clinical records is probably due to the fact that a great many of these tumors cause no symptoms and never come to operation. Probably about 15 to 20 per cent of tumors of the stomach are benign.

The authors discuss 108 cases of benign gastric tumor seen at Bellevue Hospital. Of these, 76 were only found on microscopic examination at autopsy. Forty-two of these patients had been free of symptoms while in 18 the symptoms suggested ulcer, gastritis or malignant tumor. As a matter of fact, these conditions frequently coexist with benign tumors of the stomach. This of course makes diagnosis difficult.

In 30 per cent of the other 32 cases, the diagnosis was made before operation while in the others it was made during operation. Half of the latter group of cases had been diagnosed as carcinoma. The roentgen findings may closely resemble those of carcinoma.

Gastric hemorrhage (seen in 40 per cent of the cases) was the most frequent symptom. It resembles the massive hemorrhage of ulcer rather than the slow bleeding of carcinoma. There was obstruction of the pylorus in about 30 per cent of the cases which was frequently intermittent. In roentgenograms of these cases a filling defect with gastric residue often gave a picture resembling that of carcinoma.

Eight cases of different types of benign tumor of the stomach are described in detail and illustrated with roentgenograms and photomicrographs.

All benign tumors of the stomach should be treated surgically because of the danger of severe hemorrhage and malignant degeneration. Local excision is sufficient for most of the types of tumor but the percentage of malignant degeneration is unusually high in sessile adenomatous polyps at the pylorus. Resection of the stomach is indicated in this group of cases.—*Audrey G. Morgan.*

Poppel, M. H., and Starr, S. Roentgen manifestations of acute infectious mononucleosis in the abdomen. *Radiology*, Oct., 1942, *39*, 437–439.

Acute mononucleosis or acute glandular fever is an infectious disease the causative agent of which is unkhown. It occurs mostly in children and young adults and is characterized by fever, enlarged glands and particularly a monocuclear leukocytosis with a reduction of the polynuclear granular cells to from 2,000 to 4,000 per cu. mm. There is a specific agglutination test (herterophile test) which is practically pathognomonic in high titers if the patient has not been given serum.

Abdominal symptoms are not unusual and a case is reported in this article in a male nurse twenty years of age who had been working with another male nurse who had just recovered from mononucleosis. He came to the hospital August 17, 1939, with a history of diarrhea and diffuse pain in the upper abdomen for three days. Roentgen examination showed displacement of the descending duodenum to the right and backward and a pressure defect on the lower surface of the left half of the transverse colon. These findings suggested multiple abdominal masses outside the intestinal tract in the region of the head of the pancreas. Repeated blood counts were normal. On December 3, 1939, a heterophile reaction was first obtained, showing agglutination in a dilution of 1:64. This was thought to prove the diagnosis of acute mononucleosis of the abdominal type. A month later, in January, 1940, a 5 per cent mononuclear count was found.—*Audrey G. Morgan.*

Smedal, Magnus I. Pyloric ulcers. *Radiology*, August, 1942, *39*, 200–207.

Peptic ulcers sometimes occur in the pyloric valve that show certain roentgen characteristics that differentiate them from both duodenal and prepyloric ulcers. This differentiation is very important because these pyloric ulcers are in the great majority of cases benign while the prepyloric ulcers are for the most part malignant. The author does not believe that patients with pyloric ulcer should be subjected to resection of the stomach on the chance of discovering malignant changes which exist in only relatively few of the cases.

To illustrate his point he gives roentgenograms of 10 such cases of acute pyloric ulcer. All showed certain distinctive roentgen characteristics, such as deformity of both the prepyloric area and the base of the cap; distortion and broadening of the pyloric sphincter, especially as healing takes place, and a penetrating type of ulcer crater, usually on the lesser side of the sphincter. All of these cases proved to be benign, which tends to confirm his theory.—*Audrey G. Morgan.*

Poppel, M. H., and Bercow, Celia. Perforation of peptic ulcer. *Radiology*, August, 1942, *39*, 221–225.

Perforation may be the first definite sign of ulceration and is a very serious complication. Perforations may be acute, subacute or chronic. Acute perforation may be shown on a simple abdominal film made in the upright or semi-upright position by the presence of free air under one or both halves of the diaphragm, or it may be shown by the presence of free air between the right lateral wall of the abdomen and the liver in anteroposterior films made with the patient in the left lateral recumbent position. But free air under one or both halves of the diaphragm does not necessarily prove perforated ulcer. The differential diagnosis from other conditions that produce the same effect is discussed. The administration of contrast medium is generally necessary for the demonstration of the subacute and chronic forms. Internal fistulae sometimes form gradually from perforation and are discovered by chance on the examination of old people.

A series of roentgenograms is given showing the different types of perforation seen by the authors and illustrating the diagnostic roentgen features.—*Audrey G. Morgan.*

Steigmann, Frederick. Treatment of large gastric ulcers. *Arch. Surg.*, Nov., 1942, *45*, 764–775.

The author is convinced that large ulcers of the stomach should always be operated on. While it is true that only a small percentage of gastric ulcers undergo malignant degeneration, the fact that it occurs at all makes the presence of such ulcers a risk to all patients. Neither clinical, laboratory nor roentgen examination can differentiate accurately between benign and malignant lesions. Achlorhydria may occur in patients with benign gastric ulcer and patients with malignancy may have a free hydrochloric acid up to 40 degrees. Illustrative roentgeno-

grams are given showing the impossibility of differentiation between benign and malignant ulcers by roentgen examination.

But leaving aside the question of malignancy, there is the ever-present danger of hemorrhage in large gastric ulcers. The mortality from such hemorrhages is almost 50 per cent. This is because such bleeding generally occurs in elderly people with sclerotic vessels and the vessels are apt to be embedded in scar tissue which prevents spontaneous contraction. Moreover, these ulcers heal poorly and the patients are rendered chronic invalids. These ulcers may perforate into the abdominal cavity or penetrate into neighboring organs, causing death or anatomic deformities that result in permanent invalidism, and even if they heal they may cause tobacco-pouch stomach or hour-glass stomach which require operation.

Therefore such ulcers should always be operated on at an early stage. This conclusion is based on a study of over 400 cases seen at Cook County and other hospitals in Chicago over a period of ten years.

High gastrectomy is the treatment of choice in the majority of cases. In recent years spinal anesthesia has been used most frequently in these operations.—*Audrey G. Morgan.*

Falk, Victor S. Familial polyposis of the colon. *Arch. Surg.*, July, 1942, *45*, 123–128.

A study is made of a family of 7 children, 6 of whom had congenital polyposis of the colon. The history on the maternal side was negative. The paternal grandfather died at the age of thirty of what was reported as cholera morbus. The father died at forty-eight of carcinoma of the rectum after a long history of diarrhea with blood and mucus which was suggestive of multiple polyposis.

Three of the 6 children affected were males and 3 females. In 2 of them malignant changes developed in the polyps. These patients were both males but they were also the two oldest children. The oldest of the children was thirty and the youngest ten at the time of the examination. The polyps in the ten year old girl were very small.

The 2 oldest patients who showed malignant changes were operated on and died. In the third a successful ileocolostomy was performed but she says she will not be operated on again. In the fourth a permanent ileostomy was established and she will probably submit to total colectomy later. The fifth, a boy of twenty-one, has not yet decided whether he will accept operation and the ten year old girl will be kept under observation until she is older.

The diagnosis in these cases is established by sigmoidoscopy and roentgen examination of the colon. Because of the tendency to malignant degeneration permanent ileostomy should be established and total colectomy and posterior resection of the rectum performed later.—*Audrey G. Morgan.*

Henderson, Samuel G., and Briant, W. W., Jr. The colon in the healthy newborn infant. *Radiology*, Sept., 1942, *39*, 261–272.

The authors studied the colon in 105 healthy newborn infants by means of barium enema, which is very much superior for the purpose to the barium meal. The children were given a cleansing enema in the nursery and then the opaque enema was given by passing a small rubber catheter through a hole in a rubber stopper which is passed 1½ to 2 inches into the anus and held in place by manual pressure while the enema is given. Two to 2½ ounces of barium mixture completely fill the colon of the newborn infant.

Eighty-one of the infants showed definite haustral markings, though usually they were less pronounced than in the adult. Redundancy of the colon was found in almost all cases. A table is given showing the size of lumen, degree of redundancy, position in the abdomen, length and height of the upper flexure in relation to the position of the vertebrae. There was frequently redundancy of the descending colon, splenic flexure, and transverse portion, while the sigmoid was practically always redundant in early infancy and the heptatic flexure almost as frequently. The cecum was found in the right iliac fossa in 50 per cent of the infants; in 25 per cent it was above the crest of the ilium but a true subhepatic cecum was not found. The appendix was seen in 23 cases; the terminal ileum was easily visualized.

Nineteen of the infants were re-examined after three months to one year. Conclusions cannot be drawn from so small a number of cases but redundancy of the colon was less marked in this group, probably because of growth of the body in length. Further group studies should be made of children of different ages in order to follow up the further development of the colon.—*Audrey G. Morgan.*

Bouslog, John S. The normal stomach and small intestines in the infant. *Radiology*, Sept., 1942, *39*, 253–260.

Little attention has been paid to the study of the normal gastrointestinal tract in the infant and young child. In studying the roentgen pattern of the gastrointestinal tract, the author was struck by the differences from the adult pattern. He therefore made photographic studies of the gastrointestinal tract in fetuses and infants who died at birth or shortly thereafter. Photographs, photomicrographs and roentgenograms of such tracts are reproduced.

Anatomists have generally claimed that the stomach of the newborn child lies vertically with the greater curvature to the left and the lesser curvature to the right. It is also claimed that the infant's stomach does not have a fundus. The author's roentgen examinations showed that in the infant the stomach is high in the abdomen, and usually transverse in position with the lower border of the greater curvature above the level of the third lumbar vertebra. The fundus and subdivisions of the stomach can be recognized definitely. The rugae are present and increase in development with the growth of the fetus. The musculature is poorly developed. The duodenum is not yet differentiated. Both the jejunum and ileum are small coiled narrow tubes. The pylorus is well defined. In the infant at birth there is a change in the character of the mucosal folds at the junction of the jejunum and ileum.—*Audrey G. Morgan.*

Deamer, Wm. C., and Capp, Charles S. Clinical aspects of gastro-intestinal disease in childhood. *Radiology*, 1942, *39*, 273–277.

The author discusses the clinical aspects of a number of gastrointestinal conditions in childhood which may be encountered by the roentgenologist, including celiac disease, or chronic intestinal indigestion, Hirschsprung's disease, or hypertrophy and dilatation of the colon, intussusception, peptic ulcer, Meckel's diverticulum, rheumatic abdomen, mesenteric lymphadenitis and abdominal allergy. The discussion is confined to the clinical, not the roentgen findings.

In closing the discussion on the series of articles on gastrointestinal diseases in childhood, Dr. Henderson said he had been asked "What is a normal colon?" and was obliged to answer that he did not know. The question could be answered only by serial studies on the same group of children over a period of several years. The sigmoid tends to change its position in the abdomen from time to time but this can be shown only by serial examinations. As to the question of how long the apparent elongation of the sigmoid persists, none of the children studied were examined after more than a year and he cannot give any statistics on the subject. —*Audrey G. Morgan.*

Spiesman, Manuel G., and Rubenstein, Hyman I. Hodgkin's lymphogranuloma (rectal stricture). *Ann. Int. Med.*, August, 1942, *17*, 349–358.

Hodgkin's disease of the gastrointestinal tract is rare and stricture of the rectum caused by this disease is so rare that the case reported here is the third one known. The etiology of the disease is not known.

Hodgkin's rectal structure must be differentiated from carcinoma of the rectum, lymphopathia venereum, ulcerative proctitis and colitis, amebic granuloma, tuberculous and syphilitic stricture of the rectum and post-irradiation stricture.

The authors' case was in a young woman of twenty-four who first came for treatment in November, 1931, for dry cough with no history of respiratory infection. The picture was such as to suggest either leukemia or Hodgkin's disease. Examination of an excised cervical lymph node August 4, 1932, showed the changes typical of early Hodgkin's lymphogranuloma. A biopsy from the perirenal region taken some three weeks later showed a much more advanced stage of the disease.

Deep roentgen treatment was given under which she improved greatly and the next summer (1933) she became pregnant and was delivered of a normal baby on May 17, 1934. Labor and the puerperium were moderately febrile and during the three months following delivery oliguria developed, accompanied by increasing pain in the abdomen and left lumbar region with progresssive edema of the legs. A gastrointestinal roentgen examination did not show anything abnormal.

On August 15, 1943, pyelography showed that the left kidney was not functioning. Glands were found compressing the left kidney and ureter and a biopsy specimen showed the picture of Hodgkin's disease.

Under deep roentgen treatment she improved

and gained weight until the summer of 1939 when she complained of tenesmus and mucosanguineous stools. In March, 1939, rectal examination showed a firm constricting ring in the ampulla of the rectum. Further roentgen treatment was given.

The question arises as to whether the constricting rings were caused by the Hodgkin's disease or the irradiation, but biopsy specimens showed that the Hodgkin's infiltration had extended from the abdominal and pelvic lesions.

From this time the course was retrogressive with fever, abdominal pain, tenesmus and stools containing blood and mucus, followed by progressive emaciation with bronchial congestion. The patient died January 11, 1940, more than eight years after the beginning of the disease. Autopsy was not permitted.—*Audrey G. Morgan.*

Menne, Frank R., Mason, David G., and Johnston, Robert. Lymphosarcoma of the intestine. *Arch. Surg.*, Dec., 1942, *45*, 945–956.

Tumors of the small intestine are relatively rare as compared with those of the stomach and large bowel, due to the anatomic and functional nature of the small intestine.

The authors describe 2 cases of lymphosarcoma of the small intestine. The first was in a man of forty-two who reported that he had had bilious attacks associated with nausea and vomiting since childhood. Later he had constipation necessitating excessive use of cathartics, and for three months before examination he had had a dull ache in the abdomen sometimes increasing to sharp pain. An indefinite mass was felt in the right side of the abdomen. A roentgenogram showed the terminal 8 inches of the ileum somewhat dilated, suggesting partial obstruction. The mucosa of this part of the ileum was mottled, suggesting inflammation. A diagnosis of terminal ileitis was made and operation performed. The mass found in the terminal ileum on operation proved on histological examination to be a very malignant lymphosarcoma. The terminal ileum, the cecum and a part of the ascending colon were removed and the ends of the uninvolved parts of the ileum and colon sutured together. The patient recovered after 155 days of hospitalization and is free of recurrence after four years.

The other patient was a male high school student seventeen years of age, who complained chiefly of flatus and constipation. He had atypical signs of incomplete obstruction, such as tenderness, pain, tympanites, nausea and vomiting, and a diagnosis of intestinal obstruction was made. A tumor of the ileocecal valve removed on operation proved to be a primary lymphosarcoma. The patient died and autopsy showed recurrent metastatic lymphosarcoma of the peritoneum, heart, anterior mediastinum, mesentery and retroperitoneal organs and tissue.

Only about 376 authentic cases of lymphosarcoma of the small intestine have been reported. The authors found only 1 case among 38,076 surgical tissues and 11,446 autopsies. Their second case was seen soon after this investigation was made.—*Audrey G. Morgan.*

Miller, Earl R., and Herrmann, Walter W. Argentaffin tumors of the small bowel; a roentgen sign of malignant change. *Radiology*, August, 1942, *39*, 214–220.

Carcinoids or argentaffinomas are rare tumors that originate in the argentaffin cells, so named because of their affinity for silver, found at the bases of the crypts of Lieberkühn in the gastrointestinal tract. They are generally benign and of no clinical importance. But the authors have seen 3 cases of malignant small bowel carcinoids which they describe in detail, one in a man of fifty, one in a woman of fifty-five and one in a man of sixty-seven.

Generally these patients are middle-aged, though cases have been seen at all ages from ten days up. They complain of long-standing gaseous distention, bloating, periumbilical pain and steadily increasing loss of weight. The roentgenogram shows the small bowel distended with gas and fluid up to a point of partial obstruction. Careful examination at the site of obstruction shows a small filling defect and the bowel is found to be kinked. The diagnosis is suggested by the association of kinking and tumor of the bowel.—*Audrey G. Morgan.*

SKELETAL SYSTEM

Sussman, Marcy L., and Copleman, Benjamin. The roentgenographic appearance of the bones in Cushing's syndrome. *Radiology*, Sept., 1942, *39*, 288–292.

The authors discuss 7 cases of Cushing's syndrome seen at Mt. Sinai Hospital. They were all in adult females, as the majority of cases of this disease are. The clinical features

are increased fat on the trunk, vascular hypertension, amenorrhea, purplish stripes on the abdomen, choleric facies, varying degrees of hirsutism, acneiform eruptions on the face and trunk and decreased sugar tolerance. The characteristic roentgen change is osteoporosis. Six of the authors' patients showed osteoporosis, which was most frequent in the skull but most marked in the spine and ribs. In 1 case the femora and humeri were also involved. The osteoporosis of the skull, seen in 5 of the 7 cases, was irregularly distributed, occurring most frequently in the frontal and parietal regions. The osteoporotic areas were roughly triangular in shape, or in some cases roughly circular, resembling cancer metastases.

The osteoporosis of the spine was barely visible in some cases while in others it was so severe as to have caused compression fractures of the bodies of the vertebrae. There was a characteristic change in the anterior ends of the lower ribs near the costochondral junctions. The ribs were expanded to about twice their normal size for a distance of about an inch and this area was outlined by a calcified shell. The roentgen and histological picture was that of callus.

Nearly all cases of Cushing's syndrome reported in the literature are associated with basophilic pituitary adenoma.

Four of the authors' patients presented carcinoma and 3 adenoma of the adrenal cortex, as proved on operation or autopsy.—*Audrey G. Morgan.*

Connor, Paul J., and Maier, F. Julian. The value of roentgen rays in the diagnosis of endocrine diseases. *Radiology*, Sept., 1942, *39*, 283–287.

Endocrine disturbances frequently cause changes in the bones that can be diagnosed by roentgen examination. It is important for the roentgenologist to know the nature of the bone changes in the different endocrine diseases and for all physicians to realize that they must understand the essential facts of endocrinology, no matter what their specialty.

A brief review is given of the bone changes that can be diagnosed roentgenologically in acromegaly, gigantism, dwarfism, both of the endocrine and non-endocrine types, Simmonds' disease, Cushing's syndrome, hyperthyroidism, Addison's disease, hyperadrenalism, hyperparathyroidism, the Schüller-Christian syndrome, disseminated osteitis fibrosa, Paget's disease, mongolism, pineal gland disturbance and hypogonadism. Enlargement of the thymus gland can be demonstrated only by roentgen examination. Ordinarily roentgen examination is of little value in hyperthyroidism but in long-standing cases it may show osteoporosis and often osteomalacia. It may also be possible to demonstrate a substernal thyroid by roentgen examination.—*Audrey G. Morgan.*

Barden, R. P., Belk, W. P., Pratt, G. E., and Taylor, W. R. [Ewing's endothelial myeloma with extensive skeletal involvement.] *Radiology*, Sept., 1942, *39*, 334–336.

The subject of this clinicopathological conference was a white boy five years of age who had a history of seven months' pain in the joints and intermittent fever. He had been treated for acute rheumatic fever without improvement. Laboratory examinations showed red cells 2,800,000, hemoglobin 50 per cent. The white count was 2,000, of which 68 per cent were adult lymphocytes. Roentgen examination of the skeleton showed many punched out areas of rarefaction in the skull, pelvis and the diaphyses of the femora and tibiae. All the long bones showed smooth, regular periosteal proliferation extending along the shafts. During the next two months enlargement of the spleen, liver and lymph nodes appeared. The child was given supportive and roentgen therapy but with the beginning of the eighth month began to lose ground steadily. Subcutaneous ecchymoses and persistent neutropenia developed. A week before death the white count was 300 with no polymorphonuclears. This agranulocytosis was associated with generalized furunculosis.

A study of the roentgenograms led to a roentgen diagnosis of sympathetic neuroblastoma with extensive bone metastases. A study of the bone marrow, however, showed cells like those of Ewing's endothelial myeloma and the pathological diagnosis was Ewing's endothelial myeloma with extensive bone involvement.

In the discussion Dr. Pratt said that the original blood picture led to a diagnosis of lymphatic leukemia and asked whether a leukemoid blood picture was often seen with bone metastases of tumor. Dr. Belk said he would not say it was frequent but that it might occur in children in extensive replacement of bone marrow with tumor, and it should always be considered in differential diagnosis when the

picture of aleukemic leukemia is associated with extensive destruction of bone.—*Audrey G. Morgan.*

Levitt, Abel, and Levy, Dexter S. Multiple myeloma. *Ann. Int. Med.*, Nov., 1942, *17*, 863–873.

Multiple myeloma is a form of malignant tumor with multiple foci in the red bone marrow. The etiology is unknown. The majority of cases occur in males between the fourth and sixth decades. The most important method of diagnosis is by roentgen examination of the bones, but the final diagnosis must be made by microscopic study. The blood picture is not characteristic except for a marked anemia.

A case is described in a young man of twenty-five. He was well until September, 1936, when he began to have a dull aching pain in the thighs. He thought this was only the result of over-exertion for about a year, but the pain steadily increased until he was unable to work and became sharp and stabbing. In November, 1938, he was sent to hospital. He presented marked anemia but no Bence-Jones protein in the urine. Roentgen examination showed myelomatous lesions in the skull, lumbar spine, pelvic bones and along the shafts of the femurs. He was kept in bed until his death March 23, 1940, and given treatment for the anemia and other symptomatic treatment. He suffered such intense pain that the use of narcotics was necessary.

Autopsy showed complete disintegration of most of the bones of the body. There was edema of the lower extremities caused by obstruction to venous return by the masses in the pelvis. There were metastatic calcifications of the skin and kidneys, myocardial degeneration and dilatation of the heart and edema of the lungs.—*Audrey G. Morgan.*

Menville, L. J., Williamson, L., and Mattingly, D. Renal rickets, with report of a case. *Radiology*, Oct., 1942, *39*, 410–416.

The first case of late rickets associated with albuminuria was reported by Lucas in 1883. The authors' case reported in this article brings the number of reported cases up to 128. There are two theories as to the cause of renal rickets. One is that the primary causative factor is kidney disease dating from birth or early youth and the other is that it is due to malfunction of the pituitary. The blood calcium is usually decreased in renal rickets and phosphorus increased.

Renal rickets occurs as a rule in late childhood and apparently has no sex preference. There are two types of bone changes, the rachitic type and the woolly type in which, in addition to decalcification, the trabeculae are thin and the metaphyses suggest moth-eaten bone.

The authors' case was in a white boy six years of age who was suffering from disturbed bone formation and severe anemia. For nine months he had had yellow discoloration of the skin and had steadily lost weight and strength and for the past week had been unable to stand. He gradually grew weaker in spite of blood transfusions and infusions of saline and glucose and he died five days after admission. Roentgen examinations had shown decalcification of the bones and calcification of the arteries and soft tissues. The skull showed thickening of the tables, especially at the base. A pyelogram showed no signs of calculi; there was bilateral dilatation of the pelves but the calices were small. Autopsy showed the kidneys small, pale and scarred with several small cysts on the surface and small areas of calcification in the parenchyma. Areas of focal calcification were found throughout the aorta and the common and external iliac arteries. The bones showed erosion of the cortices, decalcification and widening of the haversian canals and fibrosis and giant cells. There were hematopoietic foci in the marrow of the diaphysis of the femur and in the vertebrae.—*Audrey G. Morgan.*